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CONTENTS

I. On a New Theory of Progressive Evolution. By Karl Pearson, F.R.S. (With two plates and one figure in text.) II. Some New Pedigrees of Hereditary Disease. A. Polydactyliam and Syndactyliam. B. Blue Sclerotics and Fragility of Bone. By Julia Bell, M.A., M.R.C.P. (With two pedigrees in text and ten plates.) III. A Biometric Investigation of Twins and their Brothers and Sisters. By Percy Stocks, M.D., D.P.H., Reader in Medical Statistics, University of London. (With four figures in text.) IV. Studies of Palaeolithic Man. Part IV. A Biometric Study of the Upper Palaeolithic Skulls of Europe and of their Relationships to Earlier and Later Types. By G. M. Morant, D.Sc. (With twelve plates, sixty-three contours, a folding table of measurements, and sixty-three tissues in a pocket at the end of the part.) V. Two Pedigrees of Retinitis Pigmentosa. I. A Pedigree of Retinitis Pigmentosa. By C. H. Usher, M.B., B.Chir. (Camb.), F.R.C.S. (Edin.). II. A Pedigree of Retinitis Pigmentosa. By C. H. Usher, M.B., B.Chir. (Camb.), F.R.C.S. (Edin.) and T. Shennan, M.D., F.R.C.S. (Edin.). (With two pedigrees in text.) VI. Note on the Blood-relationship of Double Cousins. By Karl Pearson, F.R.S.

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A MODEL OF THE LEFT HALF OF THE HUMAN MANDIBLE AT THE 17 MM. C.R. STAGE

By Professor FAWCETT, M.D., F.R.S.

The sections from which this model was made were stained with Mallory's stain, the most delicate known to me for bone. Fig. 1 shows the ossified mandible (*M*) as well as many other structures, e.g. Meckel's cartilage, which is partially chondrified (MC_1) and towards its anterior end unchondrified (MC_2); the tongue (*T*) is also shown near its tip for topographical purposes: finally, the associated nerves, e.g. the mandibular (*MN*), the lingual (*LN*) with the submaxillary ganglion (*SG*), the inferior dental (*IDN*), and the mental nerves (*MN*), are introduced.

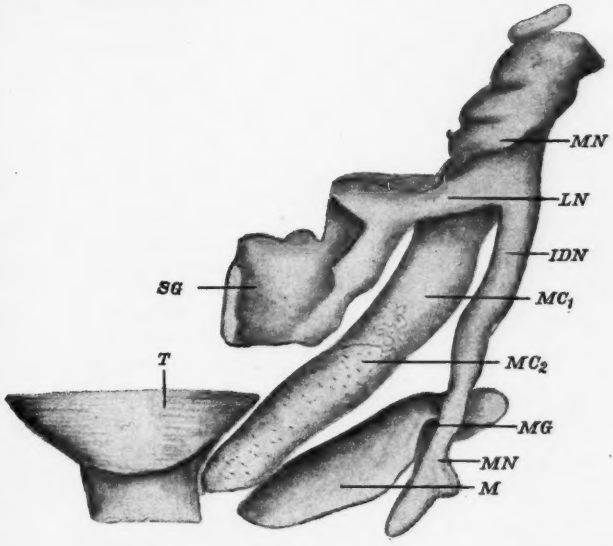


Fig. 1. Reconstruction of left mandible and annexes of a 17 millimetre human embryo viewed from above.

During the drawing for the production of the necessary wax plates a careful lookout was kept for tooth buds, but none were found. Furthermore, no sign of an incisive branch of the inferior dental nerve occurred, so the true termination of the inferior dental nerve would appear to be in the mental nerve and not a bifurcation into mental and incisive branches.

The mandible has ossified in the interval between the mental nerve and the unchondrified part of Meckel's cartilage, and it reaches from not far from the middle line to just beyond the mental nerve, which is lodged in a groove on the upper margin of the bone. The groove is the mental groove (*MG*).

The bone is a simple plate of bone with no processes. Meckel's cartilage is unchondrified from the front, back to the region of the mental groove.

The embryo from which this model was made I owe to the kindness of my colleague, Prof. D. C. Rayner.

THE THALAMUS OF *TARSIUS*

By W. E. LE GROS CLARK

Anatomical Laboratory, St Thomas's Hospital

CONTENTS

	PAGE
Introduction	371
Literature	373
Material	374
Abbreviations	374
Macroscopic features	375
Anterior nuclei	377
Medial nuclei	
N. centralis lateralis	380
N. paracentralis	381
N. dorsomedialis	382
N. submedius	383
N. parataenialis	383
N. parafascicularis	383
Centre median nucleus	384
Lateral nuclei	
Main part of lateral nucleus	387
Pars posterior of the lateral nucleus (Pulvinar)	388
N. suprageniculatus	393
Nuclei related to the optic tract	
Lateral geniculate body	395
The optic tract	399
N. pretectalis	401
Large-celled nucleus of optic tract	403
Medial geniculate body	406
Ventral group of nuclei	407
Habenular nuclei	409
Nuclei of mid-line	
N. paraventricularis	411
N. rhomboideus	411
N. centralis medius	411
N. reuniens	411
Summary	411

INTRODUCTION

In spite of intensive researches into the detailed anatomy of the brain in recent decades, we have still to admit very considerable ignorance regarding the structure and functions of the optic thalamus. There are several factors which combine to render the study of the thalamus more difficult than that of many other parts of the brain. The thalamus is made up of a rich agglo-

meration of nuclei which anatomically are often poorly defined and whose fibre connections are extremely difficult to unravel. Even such a detailed investigation as that of Gurdjian (12) on the thalamus of the rat, based upon perfectly preserved material stained by a variety of methods and sectioned in a variety of planes, yields conclusions which are of a very general and often tentative nature. The experimental method of approaching the problem involves special difficulties of its own though, indeed, this method has hardly been applied to the study of the thalamus as a whole except for the work of Sachs (26). In the case of the usual experimental animals (rabbit, cat, dog) the practical application of experimental results is hindered by the difficulties in the way of establishing homologies. A direct comparison of the complicated thalamus of, say, a dog with that of the higher Primates is hardly feasible. The elaboration and specialisation of this intricate part of the brain along divergent lines in these two examples make it well-nigh impossible to homologise all the nuclear elements of one type of thalamus with those of the other. If comparative anatomy is to be of assistance in unravelling the complexity of the mammalian thalamus, it can only do so by paying due regard to phylogenetic considerations. By studying a graded series, it is theoretically possible to compare the structure of a complicated type of thalamus directly with that of a simple type, and in this way to determine the basic plan upon which the nuclear configuration of the thalamus is built up. Having established this, it may then be possible to compare the various complicated types of thalamus in different mammalian groups. Thus, for example, if it is possible to trace back the complicated structure of the thalamus of the human brain through what can be regarded as the approximate equivalent of an evolutionary series to the more simply constructed thalamus of a generalised insectivore, and so reduce the human thalamus to its simplest expression in the mammalian order, then, by following the phylogenetic development of the thalamus from this simple and generalised prototype along the various directions in which it may have developed in other specialised orders, a rational basis for ascertaining homologies in mammals of diverse groups can be established.

It is clear from the literature that there exists, so far as our present knowledge goes, a gross structural gap between the thalamus of the higher Primates and the thalamus of lower Mammals. The confusion that has resulted from attempts to recognise in lower forms the pulvinar and the centre median nucleus of higher Primates is sufficient indication of this morphological hiatus.

General anatomical considerations suggested that *Tarsius*, in many ways the most primitive existing member of the Primates, would serve to bridge this gap. The results of the studies which are incorporated in the present paper justify this supposition. Structural links between the thalamus of *Tarsius* and Man are provided by *Lemur* and *Cercopithecus*, in which forms the thalamus has been anatomically considered in some detail by Pines (24), Vogt (29), and Friedemann (11). In the opposite direction, the thalamus of *Tarsius* may be

compared detail for detail with that of such a primitive and generalised insectivore as *Erinaceus* by way of the more highly developed thalamus of *Tupaia* (7).

This paper, therefore, is essentially an attempt to bring the thalamus of higher Primates into morphological relation with that of lower Mammals by using the thalamus of *Tarsius* as a structural link between the two groups.

Attention has been confined to the thalamus proper and no detailed account has been given here of the hypothalamus and subthalamus. The main features of these difficult regions are, however, indicated in the text-figures.

LITERATURE

Although the literature dealing with the mammalian thalamus may be said to be extensive (if not voluminous), there has been, with few exceptions, no intensive study of this part of the brain until recent years. Since the classical work of Nissl (22) (thalamus of rabbit), von Monakow (20) (cat, dog, man), and Cajal (3) (rodents), the most detailed studies of the thalamus as a whole are those of Friedemann (11) (*Cercopithecus*), Vogt (29) (*Cercopithecus*), Sachs (26) (mammals generally), Winkler and Potter (30, 31) (rabbit, cat), Pines (24) (Lemur), Gurdjian (12) (rat), and Rioch (25) (cat, dog). Reference may be made to these works for a complete bibliography of the mammalian thalamus.

As regards the literature dealing with the brain of *Tarsius*, a considerable amount of work has appeared on this subject since the original monograph of Burmeister (2) on the anatomy of this small Primate. Ziehen (37) gave a short account of the macroscopic features of the brain in 1903, and later (38) dealt in a very brief manner with the main fibre tracts in the mid-brain and thalamus. Elliot Smith (9) considered the macroscopic features of the brain in more detail in his classical memoir on the brain of the Lemuroidea and first drew attention to several remarkable features by which it is characterised. In his subsequent studies in the phylogeny of the Primate brain, this distinguished author has frequently referred to *Tarsius* and has emphasised the supreme importance of this interesting animal in the consideration of such problems. Woollard (32) provided further details on the subject in his comprehensive account of the anatomy of *Tarsius*, and later dealt with the structure of the cerebral cortex (33), the lateral geniculate body (34), and certain features of the thalamus and brain stem (35). Hunter (13) described the oculomotor nucleus. The visual cortex (5) and oculomotor nucleus (6) of *Tarsius* have also been referred to by the present writer. In 1927 Tilney (27) published a paper on the brain stem of *Tarsius* based on Weigert sections cut transversely. His attempt to correlate the relative size of fibre tracts in the brain stem with the recorded notes on the habits and behaviour of *Tarsius* is, however, hardly justified by the paucity of the data dealing with the living animal. For these few data, reference should be made to a short account published in the *Proceedings of the Zoological Society of London* (4). In the present paper no

attempt has been made to enumerate the various synonyms applied to each particular group of cells by different authors. They have been provided to some extent in a previous paper on the thalamus of *Tupaia* (7), and also in the papers of Gurdjian and Rioch.

MATERIAL

The material upon which the present study is based consists of (1) toluidin blue sections, of which there were available two transverse series (frontal series 1 and 2), a sagittal and a horizontal series, (2) iron-haematoxylin sections, transverse and sagittal, and (3) a horizontal series of sections stained by the Weigert-Pal method. The text-figures were traced, so far as the outlines of the individual nuclear masses and the fibre tracts are concerned, by the help of a projection apparatus. It is important to bear in mind the precise plane in which the frontal sections have been cut in order to appreciate the relative positions of the various elements of the thalamus. Thus, by comparing them with the sagittal sections, it will be apparent that, if the horizontal plane of the thalamus be taken as the plane of the flattened dorsal surface, the frontal series 1 (text-figs. 3 to 11) is cut obliquely downwards and slightly forwards, while the frontal series of iron-haematoxylin sections (text-figs. 12 to 14) is cut obliquely downwards and backwards.

The nuclear elements of the thalamus in *Tarsius* are, in many cases, very well-defined, so that their limits can be determined with little difficulty in toluidin blue sections. The iron-haematoxylin and Weigert sections are of considerable assistance in confirming the analysis of the thalamus based on cyto-architecture and, in addition, it is possible by their use to study some of the fibre connections of the individual nuclei.

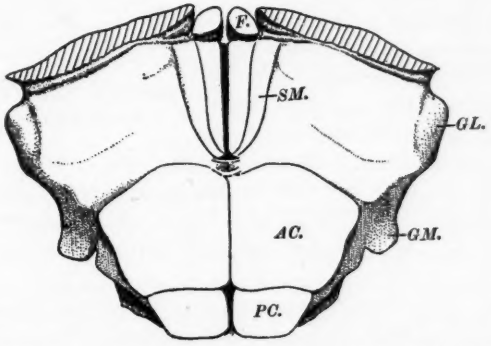
ABBREVIATIONS USED IN THE TEXT-FIGURES

A.	Main part of anterior nucleus
AC.	Anterior colliculus
Ad.	Anterodorsal nucleus
BC.	Brachium conjunctivum
BP.	Brachium pontis
CA.	Anterior commissure
CG.	Commissure of Ganser
Cl.	Nucleus centralis lateralis
CM.	"Centre median" nucleus
Cm.	Nucleus centralis medius
CMy.	Commissure of Meynert
CP.	Posterior commissure
CTv.	Ventral tegmental commissure
Ct.	Cortico-tectal tract
DB.	Diagonal band nucleus
Dm.	Nucleus dorsomedialis
Dml.	Nucleus dorsomedialis pars lateralis
Dmm.	Nucleus dorsomedialis pars medialis
DSth.	Decussatio subthalamicus
Ent.	Entopeduncular nucleus
F.	Fornix
GLd.	Dorsal nucleus of lateral geniculate body
ls.	Lamina superficialis
lc^1, *lc.*^{2}	Laminae centrales
GLv.	Ventral nucleus of lateral geniculate body
GM.	Medial geniculate body
c.	Pars centralis
l.	Pars lateralis
v.	Pars ventralis
Hbl.	Lateral habenular nucleus
Hbm.	Medial habenular nucleus
HyDm.	Nucleus hypothalamicus dorsomedialis
HyL.	Nucleus hypothalamicus lateralis
HyM.	Nucleus hypothalamicus magnocellularis
HyP.	Nucleus hypothalamicus posterior
HyVm.	Nucleus hypothalamicus ventromedialis
IC.	Internal capsule
IB.	Inferior brachium
IP.	Interpeduncular ganglion
La., *La*^{1}., *Lb.*	Main part of lateral nucleus
le.	Lamina externa
Ll.	Lateral lemniscus
Lm.	Medial lemniscus
lm.	Lamina medialis

lv.	Lamina ventralis
M.	Fasciculus retroflexus of Meynert
Mam.	Mammillary body
MFB.	Medial forebrain bundle
Mth.	Mammillo-thalamic tract
NR.	Red nucleus
OCh.	Optic chiasma
Ot.	Large-celled nucleus of optic tract
P.	Pulvinar (pars posterior of lateral nucleus)
Par.	Parolfactory area
Pc.	Nucleus paracentralis
PC.	Posterior colliculus
Pf.	Nucleus parafascicularis
Pla.	Transitional zone between main part of lateral nucleus and pulvinar
Pm.	Mammillary peduncle
Pr.	Pretectal nucleus
PP.	Pes pedunculi
Pt.	Nucleus parataenialis
Pva.	Nucleus paraventricularis anterior
Pvp.	Nucleus paraventricularis posterior
R.	Nucleus reticularis
Re.	Nucleus reuniens
Rh.	Nucleus rhomboideus
RTh.	Thalamic radiations
Sg.	Nucleus suprageniculatus
SM.	Stria medullaris
SN.	Substantia nigra
Sth.	Nucleus subthalamicus
T.	Nucleus tangentialis
TbO.	Olfactory tubercle
Tgl.	Lateral tegmental nucleus
TO.	Optic tract
TOa.	Posterior accessory optic tract
Tth.	Tectothalamic tract
Val.	Nucleus ventralis anterolateralis
Vam.	Nucleus ventralis anteromedialis
Vpl.	Nucleus ventralis posterolateralis
Vpm.	Nucleus ventralis posteromedialis
ZI.	Zona incerta
III.	Oculomotor nerve
IV.	Trochlear nerve

MACROSCOPIC FEATURES

Compared with that of *Tupaia*, the thalamus of *Tarsius* shows a significant increase in size relative to that of the mid-brain, especially in regard to transverse diameter. The greatest width is approximately 13 mm., compared with which the greatest distance between the lateral margins of the anterior colliculi is 8 mm. Viewed from the dorsal aspect (text-fig. 1), the upper surface

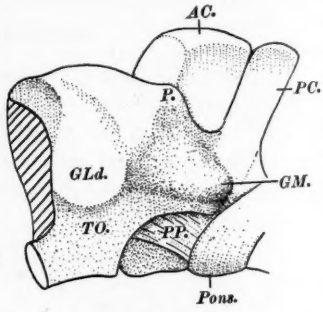


Text-fig. 1. Dorsal view of thalamus and mid-brain of *Tarsius*. × 5.

of the thalamus forms a broad, flattened area, of which the rostral margins (alongside the line of the stria terminalis) are directed laterally and with a slight obliquity caudally, while the lateral margins run medially as well as caudally. The surface is thus rather broader in front (reaching to 12 mm.) than at its most caudal level (9 mm.). The stria medullaris can readily be identified passing caudally to the region of the epiphysis as a white strand, medial to which is the habenular grey matter. The dorsal surface otherwise

shows little of note except for a low convexity anteriorly which corresponds to the anterior part of the lateral nucleus (there is no sign of an anterior tubercle associated with the position of the anterior nucleus), and a faint groove about two-thirds of the way back from the anterior margin which is directed laterally and slightly caudally, and which is the imprint of the medial border of the occipital neopallium. The antero-posterior length of the thalamus in the mid-line (extending from the foramen of Munro back to the posterior commissure) is 3·75 mm. The geniculate bodies are visible from the dorsal aspect, projecting laterally as conspicuous tubercles, the lateral geniculate body about 2·5 mm. in antero-posterior diameter, and the medial about 1 mm. in width. The latter, though smaller, is more circumscribed and relatively more prominent.

From the lateral aspect (text-fig. 2) the broad optic tract can be seen passing dorsally and caudally and spreading out over the region of the geniculate bodies. The greatest convexity of these bodies is situated on a prominent horizontal ridge which serves to divide the dorsal from the ventro-lateral surfaces of the thalamus. Postero-superiorly to the lateral, and dorsal to the medial geniculate body, the dorsal surface of the thalamus projects caudally to a slight degree to form a low convexity which topographically corresponds to the posterior pole of the optic thalamus of human anatomy (the "pulvinar"). In the undisturbed brain the anterior margin of the pons is closely applied to the tuber cinereum and the medial margin of the temporal lobe, so that the cerebral peduncles and the mammillary region are not visible unless these parts are pulled apart by manipulation. With a hand lens a distinct *tractus peduncularis transversus* can be seen crossing obliquely the crura cerebri in the usual manner.

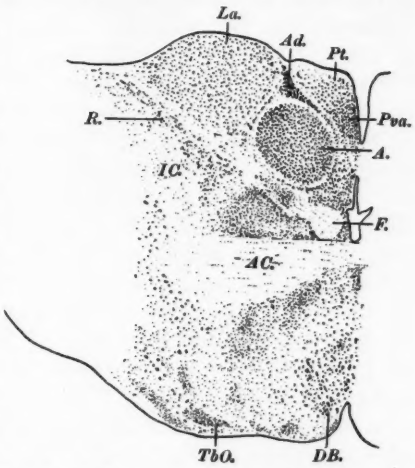


Text-fig. 2. Lateral view of thalamus and mid-brain of *Tarsius*. × 5.

The accompanying text-figures illustrate the relative proportions of the mid-brain. The prominent and somewhat cuboidal anterior colliculi fit into the deep fossa on the medial surface of the occipital lobe of the cerebrum, in the depths of which are to be found the calcarine fissures. The posterior colliculi, though much smaller, reach practically to the same height as the anterior colliculi and therein display a marked difference from the condition found in *Tupaia*. In antero-posterior diameter, the thalamus (measured from its most rostral plane to the posterior pole of the dorsal surface just noted) is slightly longer than the antero-posterior diameter of the tectum.

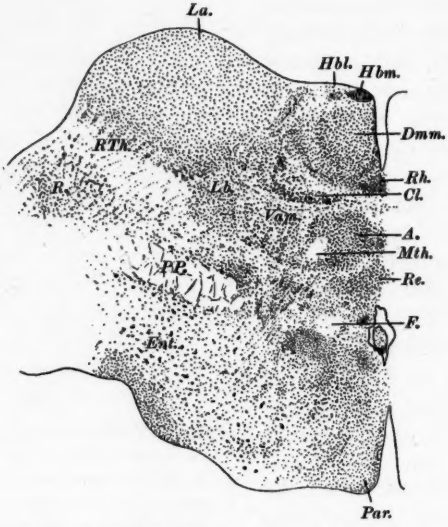
ANTERIOR NUCLEI

A very conspicuous feature in frontal sections through the anterior third of the thalamus of *Tarsius* is a sharply defined, almost circular group of closely packed cells which lies near the dorsal surface and close to the median line (text-fig. 3, *A.*). This nucleus here corresponds morphologically to the antero-ventral nucleus of lower Mammals. It is composed of medium-sized cells. In sagittal and horizontal sections (text-figs. 15 and 16) it is oval in shape, with the long axis directed vertically and transversely respectively. In width it reaches a diameter of rather more than 1·5 mm. The nucleus is abruptly circumscribed by a capsule of myelinated fibres, derived in the main from the superior thalamic radiations and the olfacto-habenular tract. The fibres of the latter, on their way dorsally to contribute to the stria medullaris, pass mainly anteriorly, but also on the lateral and medial aspects of the nucleus. In toluidin blue sections the capsule appears as a narrow, clear zone, into which extends (in rostral planes) a thin band of cells which appear to be derived from an extension of the antero-dorsal nucleus. Rostrally, the nucleus is only separated from the dorsal surface of the thalamus by a small cap of cells, the antero-dorsal nucleus, and medially by the parataenial nucleus. Laterally, at this level, it abuts upon the anterior part of the lateral nucleus, while medially it is separated from its fellow of the opposite side by an interval occupied by small raphe cells, which here forms the nucleus dorsalis raphae, or interparataenial nucleus. Traced caudally in frontal sections the nucleus sinks away from the dorsal surface of the thalamus and, at the same time, approaches the median line, where it comes into close contact with the nucleus of the opposite side (text-fig. 4). Here, at its caudo-ventral extremity, the nucleus lies medial to the anterior end of the ventral group of nuclei and is bounded ventro-medially by the n. reuniens of the middle line. No differentiation of this nucleus on the basis of cyto-architecture can be detected, except that in its middle and caudal parts the lateral portion of the nucleus, where it is penetrated by fibres of the superior thalamic radiations



Text-fig. 3. Transverse section of the thalamus of *Tarsius* at the level of the anterior nuclei and the anterior commissure. (1.) The plane of this section and of the sections shown in the following six figures is indicated in text-figs. 21 and 22. The numbers in brackets refer to the numbers of the planes. Section 16. Fr. Series No. 1. ×10. Toluidin blue.

and mammillo-thalamic fibres, is composed of cells which are somewhat smaller and more loosely packed than elsewhere. In the Weigert sections the lateral aspect of the nucleus is seen to be richly penetrated by fasciculi derived from the thalamic radiations. As these bundles traverse the nucleus, they break up into a fine medullary network which is continuous with that of the opposite side, although no distinct commissure of transversely running fibres is to be seen. Caudo-ventrally, the bundle of Vicq d'Azyr enters the nucleus and breaks up into a brush of fibres which can be traced towards its dorsal surface (text-fig. 18). In frontal sections stained with toluidin blue this bundle may first be seen (as the sections are traced caudally) in the lateral part of the nucleus.



Text-fig. 4. Transverse section at level of caudal extremity of anterior nucleus and rostral extremity of ventral nuclei. (2.) Section 72. × 10. Toluidin blue.

From this description it would appear that the element identified as the antero-ventral nucleus on topographical grounds is a large nucleus, which extends from the dorsal surface of the thalamus antero-dorsally to the ventral nuclei caudo-ventrally. Such an identification, however, leads to difficulties when comparison is made with other forms, for the nucleus is found to occupy a topographical area which is usually occupied by the antero-ventral nucleus, antero-medial nucleus, and the nucleus submedius (n. medioventralis). Certainly, if the whole of this nucleus is the morphological equivalent of the antero-ventral nucleus, there appears to be no distinct element which corresponds to the antero-medial nucleus. The nucleus just described may be called provisionally the main part of the anterior nucleus, a term which does

not imply homologies with any one particular element of the anterior group of nuclei in other forms. It must be noted that, on the basis of cyto-architecture, there is to be observed no interruption or differentiation in the antero-posterior extent of this nucleus. In iron-haematoxylin sections, also, the whole nucleus appears to be enclosed in a capsule of fibres which is continuous, though not so definite on the caudal aspect as elsewhere. On the other hand, in sagittal sections near the mid-line (text-fig. 18), the caudal part of the nucleus, which is covered dorsally by the n. centralis lateralis, bulges backwards from the main part of the nucleus and, moreover, is indistinctly marked off from the latter by small fasciculi of the thalamic radiations proceeding in a dorsal direction. Possibly this part should be regarded as the equivalent of the antero-medial nucleus. Further, in the frontal section shown in text-fig. 4, the caudal part of the anterior nucleus recalls in its position and its relation to the bundle of Vicq d'Azyr the n. submedius as shown, for instance, in Rioch's figs. 4 and 5 of the thalamus of the dog (25). It also resembles, however, the element described in *Macroscelides* (8) as the antero-medial nucleus, in the substance of which the bundle of Vicq d'Azyr runs in a similar fashion, and in which fibres of this bundle were found to terminate. An important consideration is the relation of the caudal part of the anterior nucleus of *Tarsius* to the mammillo-thalamic tract, and this question seems to be settled by the fact that, in sagittal sections, faint indications of fibres can be seen passing up to it from the tract (text-fig. 18). The question arises, therefore, whether there is a single, practically undifferentiated element in *Tarsius* (here called the main part of the anterior nucleus to differentiate it from the antero-dorsal element) which, in other forms, is split up into antero-ventral, antero-medial and, possibly, submedial nuclei. In this connection it is of interest to note that Rioch (25) describes the n. submedius of carnivores as being rostrally "more or less continuous with the ventral extension of the nucleus anteromedialis." But Dr Rioch has informed me in a private communication that he has not been able in his material to trace any direct terminal connections between the mammillo-thalamic tract fibres and the n. submedius of the cat and dog. If the n. submedius is not represented by the caudal end of the anterior nucleus in *Tarsius*, it can only be represented by scattered cells lying immediately behind the latter as suggested below (p. 383). Pending further studies of the comparative morphology of this region of the thalamus, the problem of whether the main part of the anterior nucleus of *Tarsius* is in its entirety the equivalent of the antero-ventral nucleus of other forms, or whether it represents also (incorporated in it) other elements such as the antero-medial and submedial nuclei, must be left unsettled. It is, however, pertinent to suggest the possibility that the subdivisions *aa* and *ab* of the anterior nucleus described, for instance, in *Lemur* (24) and *Cercopithecus* (11) do not necessarily correspond to the antero-ventral and antero-medial nuclei respectively of lower forms for, in *Tupaia* (7), where both the latter nuclei may be identified, the antero-ventral element

shows a tendency to be split into two parts which resemble in appearance the nuclei *aa* and *ab* of the higher Primates.

The *antero-dorsal nucleus* is readily identified in the rostral sections of the transverse series as a cap of densely packed cells covering the dorsal aspect of the antero-ventral element (text-fig. 3, *Ad.*). The cells are conspicuous for their rather larger size and deeper staining when compared with those of the antero-ventral nucleus. Anteriorly it reaches to the dorsal surface of the thalamus between the lateral nucleus and the parataenial nucleus. Ventrally it appears to be continued on either side into the capsule of the antero-ventral nucleus as a thin layer of small cells. The medial extension is directed towards the median line in sections immediately caudal to that shown in text-fig. 3, but no complete commissural nucleus can be seen connecting the nuclei of both sides. In Weigert sections the position of the nucleus is occupied by a rich network of fibres which are connected with the stria medullaris. It was not possible to follow fibres of the mammillo-thalamic tract into the nucleus.

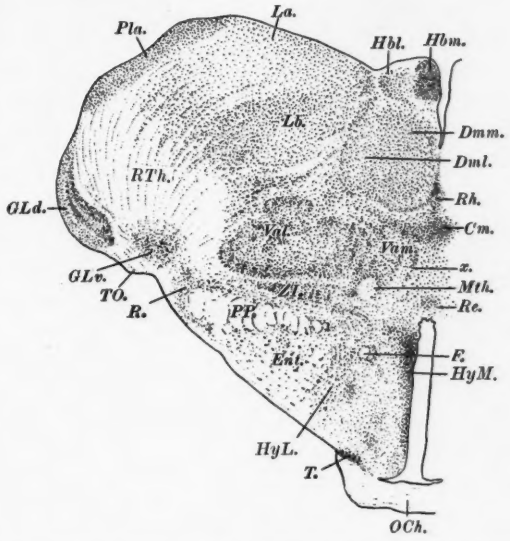
MEDIAL NUCLEI

Nucleus centralis lateralis (*Cl.*)

A few sections (about ten or so) caudal to the level at which the antero-dorsal nucleus disappears, there appears at the dorso-lateral margin of the antero-ventral nucleus a bunch of cells which are similar to those of the antero-dorsal nucleus except that they are larger. Indeed, on first inspection, they were taken to be a caudal extension of this nucleus. There is, however, a definite gap between the two groups and, as just noted, a difference in the size of the constituent cells. The posterior group is evidently the equivalent of Rioch's n. centralis lateralis (25) (Monakow's n. magnocellularis), and may conveniently be called by this name. It is to be noted that Malone (18) includes both the antero-dorsal nucleus and the n. centralis lateralis in his n. reuniens. In *Tarsius* (text-fig. 4) the group quickly extends medially, in caudal planes, to form a transverse band of cells reaching towards the mid-line and ultimately becoming continuous with the n. centralis medius. The position of this band is occupied (as seen in Weigert sections) by fine medullated fibres which cross the mid-line and thus form a distinct commissure. Its relation to the underlying caudal part of the antero-ventral nucleus in *Tarsius* suggests that the latter may be the equivalent of the n. submedius of other forms. Whether the n. centralis lateralis may be considered as a part of the same thalamic element as the antero-dorsal nucleus is perhaps worth considering for, in several features, it shows a remarkable resemblance to the n. commissuralis interanterodorsalis which forms such a conspicuous feature in the thalamus of *Macroscelides* (8). In this insectivore this commissural nucleus is directly continuous with the large antero-dorsal nucleus, is composed of the same type of very characteristic cells and, moreover, receives terminal fibres from the mammillo-thalamic tract. The relations of the n. centralis lateralis in *Tarsius* are sufficiently indicated in text-figs. 4 and 16.

Nucleus paracentralis (*Pc.*)

This nucleus is to be regarded as essentially an interstitial nucleus developed in the course of the fibres forming the medial medullary lamina, and as a commissural nucleus along which commissural fibres pass which connect up the dorsal parts of the thalamus of both sides. It is composed of small cells which laterally extend upon the lateral aspect of the dorso-medial nucleus, and medially is continuous with the n. rhomboideus and, ventrally to this, with the n. centralis medius. It can in *Tarsius* be generally distinguished from

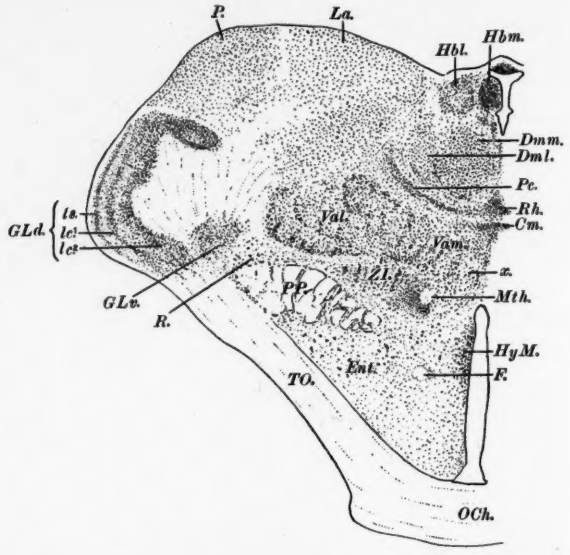


Text-fig. 5. Transverse section at level of rostral margin of optic chiasma and of lateral geniculate body. (3.) Section 120. × 10. Toluidin blue.

the n. centralis lateralis (which forms its own commissural nucleus with the n. centralis medius) by its smaller cells and its more dorsal position (text-figs. 6, 16). In parasagittal sections the paracentral nucleus appears as a band of cells running obliquely upwards and forwards towards the dorsal surface of the thalamus between the dorso-medial nucleus and the medial part of the lateral nucleus above and behind, and the lateral central, anterior and ventral nuclei below and in front. The relation of the caudal part of this nucleus to the centre median nucleus has already been noted. The paracentral nucleus as described in *Tupaia* (7) probably includes the representative of the n. centralis lateralis. The differentiation between these two elements in this insectivore cannot be made as in *Tarsius*.

Nucleus dorsomedialis (*Dm.*)

This nucleus forms in transverse and horizontal sections (text-figs. 5, 15) an almost spherical group of cells lying close to the dorsal surface of the thalamus and closely circumscribed by the medial medullary lamina. In sagittal section it is triangular with a dorsal approximately horizontal margin, a posterior vertical margin limited by the fasciculus retroflexus, and a ventral margin which slopes downwards and backwards on the dorsal aspect of the obliquely disposed paracentral nucleus. Dorsally the nucleus is in relation throughout its extent with the stria medullaris and the habenular nuclei.



Text-fig. 6. Transverse section through optic chiasma and rostral third of lateral geniculate body. (4.) Section 148. ×10. Toluidin blue.

Laterally it is related to the main part of the lateral nucleus, but separated from it by the medial medullary lamina and intercalated cells which represent the lateral upturned extremity of the paracentral nucleus. Cyto-architecturally the nucleus may be divided into two parts, one of which forms the main bulk of it and consists of cells of medium size, angular in shape and staining well. They resemble closely the cells of the main part of the anterior nucleus, except that they are more scattered and somewhat irregularly dispersed. This part appears to correspond morphologically to the large-celled element of the nucleus described by Friedemann and Pines (11, 24). It is not to be distinguished by its fibre content, however, as is the case in *Cercopithecus* and *Lemur*. The peripherally situated cells are smaller than those in the centre and are disposed

somewhat concentrically among fibres which encapsulate the nucleus. Laterally is a small-celled element of the nucleus (*Dml.*) in which the cells are more irregularly arranged and more closely packed. This part represents the lateral part of the nucleus in higher Primates, which is relatively much more conspicuous and larger in *Cercopithecus* than in *Tarsius* while, in these respects, *Lemur* seems to occupy an intermediate position. The cells on the ventral and lateral aspects of the dorso-medial nucleus are intimately related to the paracentral nucleus, the latter forming in part a commissural nucleus connecting the dorso-medial nuclei of both sides.

Nucleus submedius (*n. medioventralis*)

The question of the identity of this nucleus in *Tarsius* has been discussed in connection with the anterior nuclei (*vide supra*, p. 379). It was pointed out that the caudo-ventral part of the main anterior nucleus appears to correspond topographically to the n. submedius of other forms and yet, in *Tarsius*, it forms a single unit with the rostral part of the main anterior nucleus and receives terminals from the mammillo-thalamic tract. Caudal to the anterior nucleus and between the mammillo-thalamic tract and the mid-line are found scattered cells, which are similar to those of the medial anterior ventral nucleus in size and shape, but are more loosely arranged and more lightly stained (text-figs. 5, 6, *x.*). It is possible that this ill-defined group is the equivalent of the n. submedius. The homology must, however, be left unsettled pending further studies into the relation of the n. submedius in other forms to the anterior group of nuclei.

Nucleus parataenialis (*Pt.*)

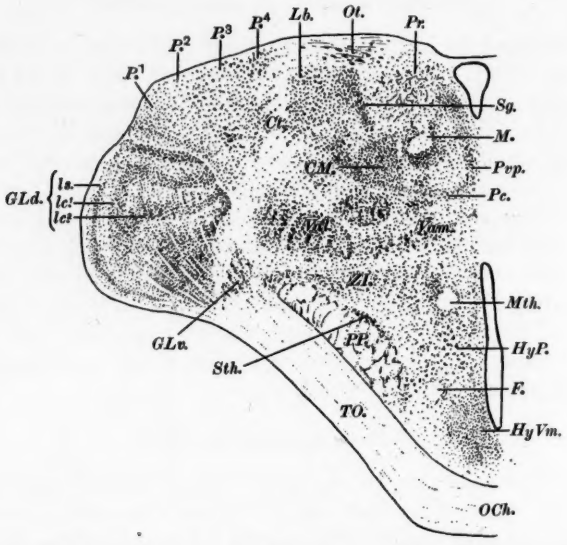
This small group of cells lies among the fibres of the stria medullaris on the antero-dorsal aspect of the main part of the anterior nucleus reaching back as far as the rostral extremity of the medial habenular nucleus. It lies medial to the antero-dorsal nucleus and the anterior end of the main part of the lateral nucleus, and in sagittal sections it is seen to be separated from the rostral pointed extremity of the dorso-medial nucleus by the antero-dorsal end of the paracentral nucleus. Medially it lies up against the paraventricular nucleus but is distinguished from the latter by its larger and more scattered cells. On the other hand, the cells of the parataenial nucleus are somewhat smaller and more lightly stained than those of the main part of the anterior nucleus.

Nucleus parafascicularis (*Pf.*)

This nucleus shows the usual characters and its general extent is sufficiently indicated in text-figs. 8, 15, 16. Its relation to the centre median nucleus has already been noted. It is richly penetrated by tecto-thalamic connections.

Centre median nucleus (*CM.*)

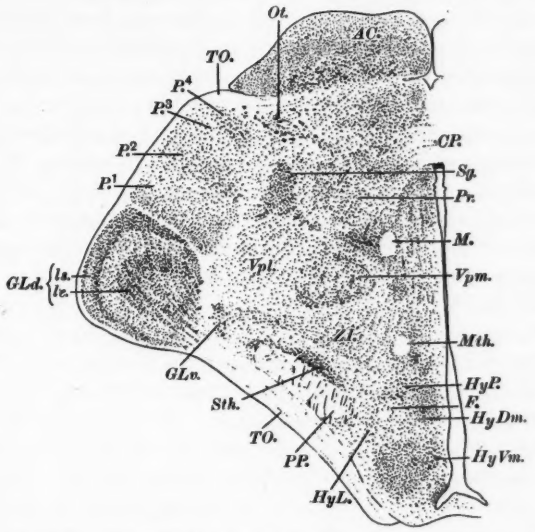
This nucleus, as is well known, forms a very conspicuous element in the thalamus of Man and the higher Primates. There has been a considerable amount of confusion in the literature of the thalamus regarding its homologies in lower Mammals, for the reason that comparison has been made usually between higher Primates and specialised animals of other orders without reference to a graded series of forms which might serve morphologically to link up the two groups, and without adequate criteria by which this nuclear



Text-fig. 7. Transverse section through optic chiasma, middle of lateral geniculate body and immediately caudal to upper end of the habenulo-peduncular tract. (5.) Section 176. ×10. Toluidin blue.

element may be identified. No better instance could well be adduced to illustrate the hopelessness of trying to homologise thalamic nuclei without any reference to phylogenetic considerations. The centre median nucleus has been described and figured in *Cercopithecus* (11) and *Lemur* (24). It is not nearly so well-defined in the latter as in the former. In these forms it appears as a group of characteristic, light-staining cells, which is situated immediately antero-lateral to the fasciculus retroflexus and the n. parafascicularis and in the course of the fibres which form the caudal extremity of the medial medullary lamina. It is surrounded by the dorso-medial nucleus dorso-medially, the posterior end of the lateral group of nuclei dorso-laterally, the ventral nuclei ventrally and ventro-laterally, the n. parafascicularis postero-medially, and

the pretectal area postero-dorsally. In the thalamus of *Tarsius* there is a similar group of cells in precisely the same relative position. Thus the frontal sections show in the caudal region of the thalamus immediately antero-lateral to the upper end of the habenulo-peduncular tract a well-defined group of cells which are clearly distinguished from cells of neighbouring groups by their smaller size, paler staining, rounded shape, and by the fact that they are closely packed together (text-figs. 7, 15). Moreover, the group is in many sections very distinctly isolated by a surrounding clear fibre zone. It can be identified as a distinct element between sections 156 and 180 of frontal series 1. Rostrally



Text-fig. 8. Transverse section through front of anterior colliculus and immediately caudal to posterior margin of optic chiasma. (6.) Section 216. ×10. Toluidin blue.

it appears in the medial medullary lamina as a differentiation of the caudal part of the paracentral nucleus and, indeed, the posterior extremity of this nucleus seems to be a commissural nucleus which links up the groups of both sides. Immediately rostral to the section shown in text-fig. 7, the nucleus appears as a circumscribed triangular group of cells bounded by the posterior end of the dorso-medial nucleus dorso-medially, by the main part of the lateral nucleus dorso-laterally, and by the ventral nuclei ventrally. At the transverse level at which the parafascicular nucleus is first apparent, the latter is sharply differentiated from the centre median nucleus by its larger, more angular, and more deeply staining cells, and it is also separated by a clear fibre zone. Caudally, however, the cells of the two nuclei freely intermingle. This relation of the caudal part of the centre median nucleus to the n. parafascicularis is also to be noted in *Cercopithecus* and *Lemur*. Weigert sections

of the thalamus of *Tarsius* also give the centre median nucleus an appearance which is precisely similar to that of *Lemur*. It is richly penetrated by medullated fibres from the medial medullary lamina and from the tectum. These fibres form a delicate but dense plexus which appears to connect the centre median nucleus with adjacent nuclei, and especially the dorso-medial, lateral, suprageniculate, parafascicular and pretectal nuclei. Woollard (35) notes that the centre median nucleus is present in *Tarsius* but, in order to avoid misapprehension, it is important to observe that this nucleus does not occupy precisely the position which is indicated in his figure.

A consideration of the cyto-architecture, topographical position and fibre relations of the centre median nucleus of *Tarsius* and especially a comparison of its appearance in sections with the centre median nucleus of *Lemur* and *Cercopithecus* leaves little doubt that they are homologous structures. In the higher Primates the only difference to be noted is its larger size and its displacement to a rather more ventral position which is clearly due to the greater size of the dorso-medial nucleus which immediately overlies it. Further, a comparison with the same region of the thalamus in *Tupaia* corroborates the opinion which was expressed previously (7), that the triangular mass of cells which appears as a differentiation of the caudal part of the paracentral nucleus in this insectivore, and which was described and figured (Plate II, fig. 5) in the paper just referred to, is the equivalent of the centre median nucleus of Primates. It may be inferred, therefore, from a consideration of the series *Tupaia, Tarsius, Lemur, Cercopithecus, Homo*, that the centre median nucleus, which is such a conspicuous feature of the human thalamus, arises primarily as a differentiation and elaboration of the caudal part of the paracentral nucleus (which here may be regarded as an interstitial nucleus developed in the track of the fibres forming the medial medullary lamina). It is developed, thus, in the direct course of a complicated system of fibre connections, which probably brings into relation with each other and with the tectum most, if not all, of the nuclear elements which make up the dorsal moiety of the thalamus. It may be regarded as an integrating mechanism related to the functions of that part of the thalamus in which progressive differentiation and growth are most obtrusive in the higher Primates. Its great development in the human brain is explicable from this point of view.

LATERAL NUCLEI

This nuclear group occupies a broad area on the dorsal surface of the thalamus between the anterior and dorso-medial nuclei medially and the geniculate bodies laterally. It is readily divisible into two main portions, the main part of the lateral nucleus antero-medially and the pars posterior (pulvinar) postero-laterally. These two portions are clearly separated by conspicuous bundles of fibres running between the internal capsule and the tectum (and presumably consisting largely of cortico-tectal connections) except anteriorly where they are joined by an uninterrupted band of cells (text-fig. 5, *Pla.*).

Main part of lateral nucleus

The main part of the lateral nucleus appears rostrally in transverse sections as a homogeneous mass of cells which lies immediately dorso-lateral to the rostral part of the antero-ventral nucleus, and which here raises up the dorsal surface of the thalamus to form a rounded eminence. It is bounded ventro-laterally by the internal capsule and the n. reticularis. In this region its cells are a little larger and more loosely packed than those of the antero-ventral nucleus. Laterally they tend to arrange themselves in ill-defined rows, parallel to the penetrating bundles of fibres from the thalamic radiations. In more caudal sections (text-figs. 4, 5) the nucleus rapidly enlarges and, as the antero-ventral nucleus becomes displaced ventrally, it comes up against the lateral aspect of the dorso-medial nucleus from which it is separated by the medial medullary lamina. Ventrally it extends deeply towards the anterior extremity of the ventral group of nuclei. The deeper part of the lateral nucleus is richly penetrated by the thalamic radiations (in contrast to the dorsal part which, in Weigert sections, forms a relatively clear area) and here, moreover, the cells are more irregularly disposed and generally more closely packed. On these grounds, the main part of the lateral nucleus may for descriptive purposes be divided into a dorsal part (*La.*) and a ventral part (*Lb.*). Further, especially in sagittal and horizontal sections (text-fig. 17; Plate I), the rostral end of *La.* is seen to be demarcated off from the remainder of this part by fascicles of fine fibres which run laterally and postero-laterally from the medial medullary lamina. The cells of this portion (labelled in the figures *La*[1].) are paler and a little larger than those in the more caudal part of n. lateralis a.

In the transverse plane in which the lateral geniculate body first appears rostrally (text-fig. 5), a narrow band of cells extends laterally from n. lateralis a. over the surface of the thalamic radiation towards the lateral geniculate body. This forms a narrow isthmus which links up the main part of the lateral nucleus with the pars posterior of the lateral nucleus (pulvinar), and probably corresponds to what Friedemann has called "Stelle des Pulvinar" in *Cercopithecus* (11). Caudally to this band, the main part of the lateral nucleus and the pars posterior are, as already noted, separated by a conspicuous medullary lamina. As the pars posterior of the lateral nucleus expands in a caudal direction (text-figs. 6, 7), the main part of the lateral nucleus progressively diminishes until, at the level of the posterior commissure (text-fig. 7), it sinks below the surface. This part appears to correspond to the posterior extremity of n. lateralis b. It is here covered in dorsally by the mesencephalic fibres of the optic tract and its large-celled nucleus. Medially to it is the dorsal extremity of the pretectal nucleus, and laterally, separated by a broad medullary lamina, the pars posterior of the lateral nucleus or pulvinar. Ventro-medially is the centre median nucleus. At this level, the medially placed cells of the lateral nucleus become more closely packed together and take on a deeper stain. This characteristic group of cells becomes displaced ventrally in more

caudal planes and forms a particularly circumscribed nucleus, the n. suprageniculatus. In horizontal sections, the cells of the main part of the lateral nucleus show a tendency to an arrangement in rows parallel to the thalamic radiations which penetrate it (text-fig. 15).

The attempt to homologise the different elements of the main part of the lateral nucleus in *Tarsius* with those described for other forms is not easy, by reason of the fact that these elements are not sharply differentiated from each other. On the basis of myelo-architecture, it seems that the divisions *La.* and *Lb.* correspond broadly to the parts which are similarly labelled in *Cercopithecus* and *Lemur* (11, 24). If this is so, then the main part of the lateral nucleus in higher Primates is characterised by a great relative increase in the proportions of n. lateralis b.

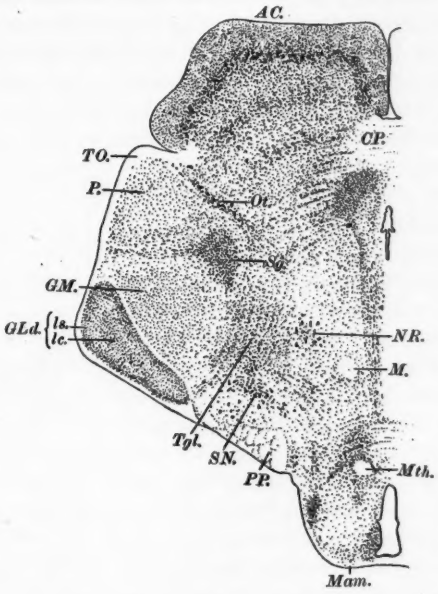
The element described as n. lateralis anterior in Carnivores by Rioch (25) is evidently the equivalent of n. lateralis a. of *Tarsius*. Rioch's n. lateralis intermedius and n. lateralis pars posterior correspond to the middle and caudal parts of the main part of the lateral nucleus in *Tarsius*. The relation of his pars posterior to the n. suprageniculatus satisfactorily establishes this homology.

Pars posterior of the lateral nucleus (*Pulvinar*) (*P.*)

It has already been noted above that, at the transverse level of the rostral margin of the lateral geniculate body, n. lateralis a. extends laterally, dorsal to the thalamic radiations, towards the lateral geniculate body (text-fig. 5). A few sections caudal to this level, this lateral extension becomes cut off from the main part of the lateral nucleus by a thick medullary lamina which consists mainly of cortico-tectal connections. It forms a mass of cells which expands rapidly in a caudal direction, extending ventrally between the dorsal parts of the lateral and medial geniculate bodies, and, posteriorly, between the anterior colliculus and the medial geniculate body (text-figs. 21 C, 22 C). A comparative study indicates clearly that it is the equivalent of the pars posterior of the lateral nucleus as described by Gurdjian in the rat (12) and by the present writer in *Tupaia* (7). This homology is attested by numerous considerations. The topography of the nucleus relative to other thalamic nuclei is precisely that of the pars posterior of the lateral nucleus in lower Mammals as can best be seen from the reconstructions shown in text-figs. 21 and 22. Its relation to the two geniculate bodies, the anterior colliculus, and the large-celled nucleus of the optic tract should especially be noted. As is the case with the pars posterior of the lateral nucleus, also, it is covered caudally by the mesencephalic root of the optic tract many of whose fibres penetrate it in conspicuous bundles, while medially it is separated from the main part of the lateral nucleus by a medullary lamina[1] formed of cortico-

[1] This medullary lamina separating the pars posterior from the main part of the lateral nucleus is visible on the dorsal surface of the thalamus of a well-preserved brain of *Tarsius* as a white strand extending anterolaterally.

tectal fibres (text-figs. 13, 14). Comparison of the figures here given of the nucleus in *Tarsius* should be made with those of the brain of the rat in Gurdjian's paper, and of *Tupaia* (7). The type of its component cells is similar to those of the main part of the lateral nucleus in general. Gurdjian (12) emphasises that in his preparations internuclear fibres between the pars posterior of the lateral nucleus and the dorsal nucleus of the lateral geniculate body are very evident. Similar connections may be also detected in our preparations of *Macroscelides* and *Erinaceus*. In *Tarsius*, also, it is clear that abundant fibres run between the lateral geniculate body and the nucleus termed the pars posterior of the lateral nucleus. Further, cortical projection fibres stream out from the antero-medial aspect of the pars posterior in



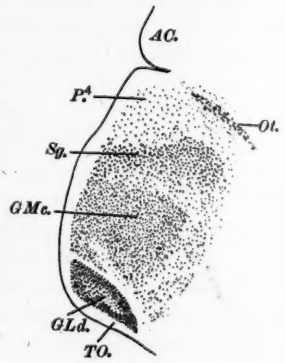
Text-fig. 9. Transverse section through anterior colliculus, caudal part of lateral geniculate body, rostral end of medial geniculate body, and mammillary bodies. (7.) Section 256. ×10. Toluidin blue.

Tarsius as in lower forms, and run forwards into the internal capsule immediately medial to the optic radiation. There can thus be no reasonable doubt regarding the homology here made.

Frontal sections (text-figs. 6 to 8) show that anteriorly the pars posterior of the lateral nucleus lies between the main part of the lateral nucleus and the lateral geniculate body, while posteriorly it is bounded medially by the large-celled nucleus of the optic tract, the n. suprageniculatus, and the posterior elements of the ventral group of nuclei in a dorsi-ventral direction.

Still more caudally (text-figs. 9, 10), it becomes sandwiched in between the large-celled nucleus of the optic tract and the medial geniculate body. Text-fig. 22 C shows the tendency of the pars posterior to embrace the upper pole of the dorsal nucleus of the lateral geniculate body, so that in certain horizontal sections (e.g. text-fig. 15) it is seen in two parts separated by the lateral geniculate body.

A study of the pars posterior of *Tarsius* in several planes reveals the fact that it can be subdivided into zones on the basis of both cyto-architecture and myelo-architecture. These zones form a series of laminae which are superimposed in a dorsi-caudal direction (text-figs. 7, 8; Plate I). Immediately adjacent to the lateral geniculate body is a zone (*P.*[1]) of small, round cells, which are somewhat closely packed and tend to exhibit a linear arrangement. The cells are intimately intermingled with fibres which stream into it from the thin medullary lamina separating it from the lateral geniculate body. Some of these fibres are probably optic tract fibres which skirt the margins of the dorsal nucleus of the lateral geniculate body from its superficial aspect, but these must be relatively few in number by reason of the small size of the optic tract which passes superficial to the lateral geniculate body. Weigert sections indicate clearly that most of the fibres thus entering the pars posterior must be derived from the dorsal nucleus of the lateral geniculate body itself. Abundant fibres from the peripheral medullary network in the lateral geniculate body can be traced into the thin medullary lamina between it and the pars posterior, and abundant fibres can again be traced from the lamina into the pars posterior. The profusion of these fibres compared with the thinness of the intervening medullary lamina justifies the conclusion that the majority are passing between the lateral geniculate body and the pars posterior. Moreover, these fibres can be traced through the small-celled zone of the pars posterior into the next adjacent zone (*P.*[2]). The latter consists of cells of medium size, sub-triangular and oval in shape, and with a tendency to an arrangement in rows which are directed dorsally, medially and caudally. They are much less closely packed than the small cells of the first zone. It is through this zone that the pulvinar as a whole becomes linked up rostrally with the main part of the lateral nucleus (*Pla.*). The third zone (*P.*[3]) which can be recognised consists of small cells which are, however, a little larger than those of the first zone. They are, in general, oval in shape and tend to be arranged in rows which are directed medio-ventrally. These cells lie amidst a fine network of medullated fibres, which extends medially and slightly rostrally through the cortico-



Text-fig. 10. Transverse section through geniculate bodies and pulvinar to show the relation of the nucleus suprageniculatus to these structures. Section 288. ×10. Toluidin blue.

tectal bundles and serve to link up chiefly the second and third zones of the pars posterior with the fine medullary network which pervades the main part of the lateral nucleus (Plate I). Dorso-caudally is the fourth zone of the pars posterior (***P.***^{4}). This consists of medium-sized cells, triangular in shape, and, for the most part, rather larger than those of the second zone. They show no indication of linear arrangement and are relatively sparsely scattered in a matrix which tends to take up the stain in toluidin blue preparations. This group of cells lies close to the tectum, immediately ventro-caudal to the large-celled nucleus of the optic tract (text-fig. 8). In Weigert sections (Plate I) it stands out by reason of the fact that it contains a much less dense network of myelinated fibres, and thus appears as a relatively clear area. It has direct tectal connections which cannot be traced with certainty to the other regions of the pars posterior. If it has any direct connections with the dorsal nucleus of the lateral geniculate body, they are far less obtrusive than is the case with the more ventrally situated zones and, in any case, they cannot be certainly detected in our preparations. It is the fourth zone which forms the extremity of the posterior pole of the optic thalamus in *Tarsius*.

The whole of the pars posterior of the lateral nucleus is penetrated by fibres which are derived from the optic tract or emerge from the thin medullary capsule of the dorsal nucleus of the lateral geniculate body. These fibres form compact bundles, which are most conspicuous in the more caudal regions. These bundles mainly pass through the pars posterior without apparent interruption, and emerge dorsally to contribute to and augment the mesencephalic root of the optic tract. From all parts of the pars posterior of the lateral nucleus fibres stream out in a rostro-medial direction to the internal capsule.

The interest of the pars posterior of the lateral nucleus largely lies in the problem of its relation to the pulvinar of Primates. The homologies of the latter in regard to lower Mammals have, up to now, not been finally established. Some authors, indeed (14), would maintain that the pulvinar is characteristic of Primates only and, therefore, is not represented in the thalamus of lower forms. The difficulty of searching for the homologous structure, however, will be sufficiently realised when it is noted that the pulvinar in Primates has never been in any way satisfactorily defined. Vogt (29) has defined the extent of what he calls the pulvinar in *Cercopithecus* on the basis of myelo-architecture, but this is a purely topographical definition and, even so, the boundaries are hardly distinct enough to be satisfactory for comparative purposes. Moreover, those who have studied this region in the Primate thalamus freely allow that the boundary between the pulvinar and the lateral group of nuclei is quite indeterminate, so that it may be entirely a matter of personal opinion as to whether a particular cell-group is allocated to one or the other. Broadly speaking, however, the term pulvinar is commonly applied to the group of nuclei which form the posterior pole of the thalamus of Primates and which come into close topographical relation with the metathalamus, the anterior colliculus, and the optic tract (some of whose fibres overlie and penetrate it). It is commonly regarded as functionally related to the lateral geniculate body

and connected by projection fibres mainly to that region of the cortex cerebri which is immediately adjacent to the striate area. Now, on topographical grounds alone, it is abundantly clear that the whole of the pars posterior of the lateral nucleus in *Tarsius* corresponds at least to part of what has been called the pulvinar in higher Primates. They both bear fundamentally the same relations to the metathalamus and the tectum, jutting in between the lateral and medial geniculate bodies, and caudally in between the medial geniculate body and the lateral margin of the anterior colliculus. These relations of the pars posterior of the lateral nucleus are illustrated in the reconstructions given in text-figs. 21 and 22. In *Tarsius* and lower forms (rat, insectivora) the pars posterior is, throughout the greater part of its extent, demarcated off from the rest of the thalamus by cortico-tectal tracts. A precisely similar relation in the case of the pulvinar is illustrated in Vogt's paper on *Cercopithecus* ((29) fig. 13) and in Pines' paper on *Lemur* ((24) fig. 26). That this medullary lamina does not, in these animals, form such a complete boundary line as in *Tarsius* is obviously due to the fact that, in the larger Primate brains, the tectum is very much smaller as compared to the bulk of the thalamus and the cortico-tectal bundles are therefore relatively less conspicuous. It has been noted that, in *Tarsius*, the pars posterior is continuous rostrally with the main part of the lateral nucleus, and it may be inferred that this cellular connection (*Pla.*, text-fig. 5) is equivalent to the "Stelle des Pulvinar" of Friedemann and Pines. The fibre connections between the pars posterior and the dorsal nucleus of the lateral geniculate body, and the origin from the former of cortical projection fibres which pass into the internal capsule in close association with the optic radiations, as well as the intimate relation between the pars posterior and the fibres of the optic tract, merely provide additional confirmation (if such be needed) for the inevitable conclusion that the pars posterior of the lateral nucleus in *Tarsius* is identically homologous with at least a part of the pulvinar of other Primates. This being the case, it follows that the pars posterior of the lateral nucleus in lower forms (as defined by Gurdjian (12)) is also the equivalent of the pulvinar, for there is no manner of doubt that the pars posterior in *Tarsius* is homologous with the pars posterior in the rat and *Tupaia*, etc. It thus appears that, far from being a prerogative of the Primates, the pulvinar is a common mammalian feature. At first sight, the relative size of the pars posterior in the thalamus of primitive Mammals such as the insectivora may be regarded as an objection against such an homology, but such an argument would be based upon the preconceived notion that the pulvinar represents an elaboration of the thalamus which is peculiarly characteristic of the higher Primates. Further, the relative size of the lateral geniculate bodies in the thalamus of primitive Mammals (in which the eyes have not undergone retrogressive changes) is very great as compared with the brains of higher Primates, and, if the pulvinar is regarded as a part of the cerebral mechanism associated predominantly with visual functions, it is to be anticipated that its representation in the thalamus will

be proportionately great. Moreover, in a series of insectivore brains, it will be found that there is a very obvious relation between the size of the pars posterior of the lateral nucleus on the one hand, and the size and complexity of the dorsal nucleus of the lateral geniculate body as well as the relative extent and differentiation of the area striata of the cortex on the other.

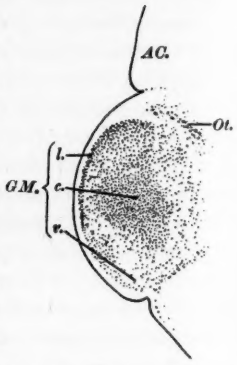
A comparative study enables the pulvinar to be defined as a caudal extension of the lateral group of nuclei which is separated from the latter to a greater or lesser degree by the cortico-tectal tracts (depending upon the relative bulk of these connections), which lies in immediate topographical relation to the lateral and medial geniculate bodies and the tectum, and whose fibre connections are predominantly with the lateral geniculate body (dorsal nucleus), tectum, main part of the lateral nucleus, and the cerebral cortex.

The difficulties of homologising the pulvinar in such simple brains as that of *Tarsius* and the insectivora with that in larger and more complicated brains are enhanced by the fact that, in the latter, the pars posterior of the lateral nucleus or pulvinar becomes displaced and rotated by the increase in size of other parts of the thalamus, especially the lateral group of nuclei. Rioch's study of this region in Carnivora shows how great this difficulty may be when an attempt is made to compare the posterior end of the thalamus in different forms. It seems probable that his pulvinar, area pretectalis, and posterior nucleus together represent the pars posterior of the lateral nucleus in lower forms and the pulvinar of Primates. If this interpretation is correct, his area pretectalis represents $P.^4$ in *Tarsius*, while his nucleus posterior, which corresponds to *Pd.* in the pulvinar of *Cercopithecus* and *Lemur*, probably is the equivalent of at least a part of $P.^1$ in *Tarsius*. Rioch's pars posterior of the lateral nucleus can hardly be homologous with the pars posterior in the rat (12), *Tupaia* (7) and other Insectivores, if only for the reason that it has not the same intimate relation with the lateral geniculate body which is so characteristic of this nucleus. I have been fortunate enough recently to discuss personally with Dr Rioch some of these problems in the homologies of the mammalian thalamus, and I would like here to express my appreciation for the aid which these consultations have been to me in my own studies in this particularly intricate subject.

Nucleus suprageniculatus (*Sg.*)

It has been noted above that the medially placed portion of the caudal extremity of the main part of the lateral nucleus becomes differentiated by the massing together of its constituent cells which here take on a deeper stain (text-fig. 7). These cells form a group which is conspicuous enough to merit the distinction of being regarded as a separate nucleus. It is termed the n. suprageniculatus, since it seems to correspond to the nucleus of the same name which has been described by Friedemann in *Cercopithecus* (at least in its caudal part), and it also fulfils all the topographical criteria of the n. suprageniculatus described by Rioch in the thalamus of Carnivores (25). In its

caudal planes, also, it compares in position and appearance with the n. parageniculatus or "noyau basale" of Vogt, in *Cercopithecus* and *Lemur*, and it may well be that this latter nucleus is a derivative of the same mass of cells. Throughout its extent, the n. suprageniculatus in *Tarsius* is closely related to the large-celled nucleus of the optic tract which lies immediately dorso-caudally to it (text-figs. 8, 9, 17). Rostrally it lies lateral to the pretectal nucleus and medial to the pulvinar, while it is in close contact with the centre median nucleus medially (text-fig. 7). Caudally it becomes displaced ventrally and laterally, and forms a remarkably well-defined element which stands out in toluidin blue sections by reason of the distinctive staining of its cells and of its separation from neighbouring nuclei by a well-marked clear area. In Weigert sections (text-fig. 19; Plate II) it can be recognised as a clear area encapsuled by cortico-tectal and tecto-thalamic bundles. In some sections the nucleus is seen to be linked up with the n. parafascicularis and the centre median nucleus by a chain of cells extending between the pretectal nucleus dorso-caudally and the lateral and ventral nuclei rostrally (text-figs. 7, 8, 15). Caudally (text-figs. 10, 11) the nucleus extends laterally between the pulvinar and the small-celled element of the medial geniculate body. It can be traced here to the surface of the thalamus between the two nuclei. Its characteristic cells then extend down on the lateral aspect of the central mass of the medial geniculate body to become directly continuous with the pars lateralis of this nucleus. In sagittal sections, also, the suprageniculate nucleus can be traced into the eminence of the medial geniculate body where it extends on to the dorsal and caudal surfaces of the latter (text-figs. 19, 20). The n. suprageniculatus in *Tarsius*, therefore, can be traced in continuity as a caudo-ventral appendage of the main part of the lateral nucleus, which ultimately becomes incorporated in the medial geniculate body. Its relation to the latter suggests an analogy with the pulvinar which, likewise an appendage of the main part of the lateral nucleus, is related primarily to the lateral geniculate body. The n. suprageniculatus, as already indicated, is remarkably free of medullated fibres. The Weigert horizontal sections, however, show a very fine plexus of medullated fibres penetrating it from the medial aspect and which proceeds from the region of the parafascicular and centre median nuclei.



Text-fig. 11. Transverse section through medial geniculate body a little caudal to that shown in the previous figure. The nucleus suprageniculatus has now extended on the lateral aspect of the body to form its large-celled pars lateralis. Section 316. × 10. Toluidin blue.

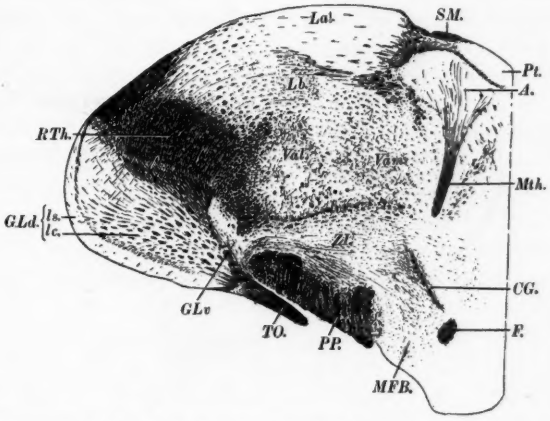
Rioch's description of the suprageniculate nucleus in Carnivores coincides very well with the condition found in *Tarsius*. He finds that it is in continuity with the medial geniculate body without, however, being able to trace

it directly into any particular component of the latter. Dorso-rostrally, he derives it from a part of his n. lateralis pars posterior, but, as already noted, the latter can certainly not be homologous with the pars posterior of *Tarsius* and other forms, and is without doubt the equivalent of the caudal portion of the main part of the lateral nucleus.

NUCLEI RELATED TO THE OPTIC TRACT

Lateral geniculate body (*GLd., GLv.*)

The lateral geniculate body in *Tarsius* forms a large and highly organised nucleus, as indeed might be inferred from a consideration of the other anatomical elements associated with visual functions in this animal. Thus, the

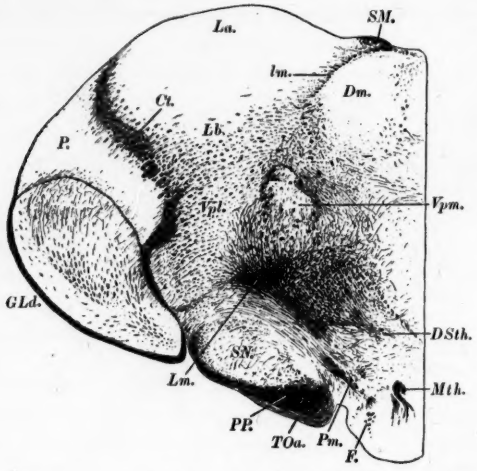


Text-fig. 12. Transverse section through anterior nucleus, rostral third of lateral geniculate body and behind the level of the optic chiasma. ×10. Iron-haematoxylin.

eyes are of a remarkable size, and, with them, the optic nerves and tracts; the retina presents a differentiation which has been regarded as the primordium of a macula lutea (34); and the *area striata* of the cortex cerebri is distinguished for its extent and the degree to which it is laminated. Woollard (34) has previously described the lateral geniculate body of *Tarsius* from a study of frontal sections stained with toluidin blue, and has noted its resemblance in structure to that of the marmoset.

Dorsal and ventral elements of the lateral geniculate body can be recognised. The ventral nucleus (*GLv.*, text-figs. 5–8, 12; Plate II) is very small relatively and lies rostral and medial as well as ventral to the large dorsal nucleus. It consists of medium-sized cells, generally sharply angular and elongated, and loosely grouped together in close relation to the termination of the most dorsally situated fibres of the optic tract. The more ventrally situated cells of the nucleus are much smaller. Medially, the ventral nucleus

is in close relation with the zona incerta to which it is connected by fine medullated fibres. The latter can be particularly well seen in the horizontal series of Weigert sections, pursuing a somewhat sinuous course through the fibres of the auditory radiations which are coursing forwards from the medial geniculate body to the internal capsule. Other fibres proceeding from the ventral nucleus pass dorso-medially into the lateral medullary lamina, presumably joining the cortico-tectal fibres therein. Although the ventral nucleus of the lateral geniculate body is obviously reduced when compared with the condition found in primitive mammalian brains such as those of the insectivora, it is much better developed in *Tarsius* than in the generality of the



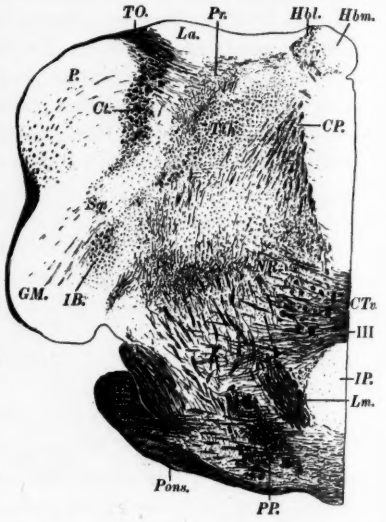
Text-fig. 13. Transverse section through middle of lateral geniculate body and corpora mammillaria. × 10. Iron-haematoxylin.

Primates (with the exception of some of the smaller lemurs such as *Perodicticus* (36) and *Chirogaleus* (15)). This is no doubt associated with the relative size of the anterior colliculus in the brain of *Tarsius* for the fibre connection of this with the ventral nucleus of the lateral geniculate body is generally recognised.

The dorsal nucleus of the lateral geniculate body (*GLd.*, text-figs. 5–9, 12, 13, etc.) has a complexity of structure which can hardly be adequately appreciated except by examining sections through it in more than one plane. As may be seen from the reconstruction in text-fig. 22 C, it is an elongated oval body situated on the lateral and ventro-lateral aspect of the thalamus, whose long axis is directed caudo-ventrally. The frontal iron-haematoxylin sections cut along the plane of the long axis (text-figs. 12, 13), while the frontal toluidin blue sections cut obliquely across it. The dorsal nucleus is a well-laminated nucleus which is deeply hollowed out to form a cup the rim of which

is somewhat turned in from the lateral aspect. In horizontal section it is thus **C**-shaped. The mouth of the cup looks forwards and medially, and out of it stream the abundant fibres of the optic radiations. All the laminae conform to this general curvature. Owing to the pronounced curvature in this direction, frontal sections may cut perpendicularly through some laminae and along the plane of others, so that the impression may be gained that there is a peripheral laminated and a central non-laminated region. For the same reason, such sections will often cut through the same laminae in two places. The peripheral or superficial lamina (*GLls.*) is more distinctly demarcated both in toluidin blue and Weigert sections than the central laminae. This peripheral lamina is a relatively thin layer of cells which are of medium size and rounded in shape. It encloses the central laminae of the dorsal nucleus, but does not extend quite so far rostrally as the latter on the dorsal and medial aspects (text-fig. 6 and Plate II). Dorso-medially, at about the middle of the nucleus (text-fig. 7), the cells are very distinctly larger and more spaced out, and here in many sections they appear as a relatively isolated band of cells. Caudally, the peripheral lamina tends to be indistinctly subdivided into two layers (text-fig. 8). The central laminae (*GLlc.*) are less sharply defined and much broader, and they fill up the centre of the nucleus. They consist of cells which are a little larger than those of the lamina superficialis and in horizontal and sagittal sections are fusiform in shape. Two central laminae may be recognised, of which the superficial (*GLlc.*[1]) encloses the deep (*GLlc.*[2]). These two layers are separated by a layer in which the cells are much less closely packed, but in front, as well as ventrally, they run into each other and become continuous. The peripheral and central laminae are separated by a well-marked medullary lamina in which a few small cells are scattered. Thus, if the zonal layer is included, there are in the lateral geniculate body of *Tarsius*, as Ziehen noted (38), three medullary and three cell layers. The main part of the optic tract reaches the lateral geniculate body at its ventro-medial pole. Here most of the fibres enter the dorsal nucleus, a minority being traced into the ventral nucleus. A small proportion of the fibres, also, pass dorsally over the lateral aspect of the dorsal nucleus towards the tectum and form thus a thin lamina zonalis. The fibres entering the dorsal nucleus break up into compact bundles which splay out in a fan-wise manner. The majority of the fibres seem thus to stream out towards the circumference of the nucleus. Ultimately they may be traced to the medullary lamina which separates the superficial from the deep cell laminae, where they break up into a fine medullary plexus, the fibres of which penetrate in among the cells of the peripheral lamina (text-fig. 12; Plate II). Many fine fasciculi may be seen traversing the peripheral lamina to reach the surface of the dorsal nucleus to enter the medullary capsule which surrounds it and to pass on thence directly into the mesencephalic root of the optic tract laterally or indirectly (on the dorsal and medial aspects of the dorsal nucleus) by passing into or through the pulvinar. It seems that at least a proportion of these latter fibres are derived from the optic tract and run an

uninterrupted course through the dorsal nucleus. While the Weigert sections suggest that the optic tract fibres are mainly distributed to the peripheral lamina of the dorsal nucleus, they also show the fibres of the optic radiations proceeding in their main bulk from the central laminae and crossing the entering optic fibres almost at right angles (text-figs. 12, 20). It is a matter of extreme difficulty to trace connections between the dorsal nucleus of the lateral geniculate body and other thalamic nuclei, for the reason that, while many fibres leaving the nucleus enter the rich medullary plexus which everywhere forms a thin capsule to the nucleus, and while many fibres may be traced from this medullary plexus into neighbouring regions of the thalamus, they cannot be traced across this capsular barrier in continuity. As indicated above, however, there is evidence of a rich fibre connection with the pulvinar.

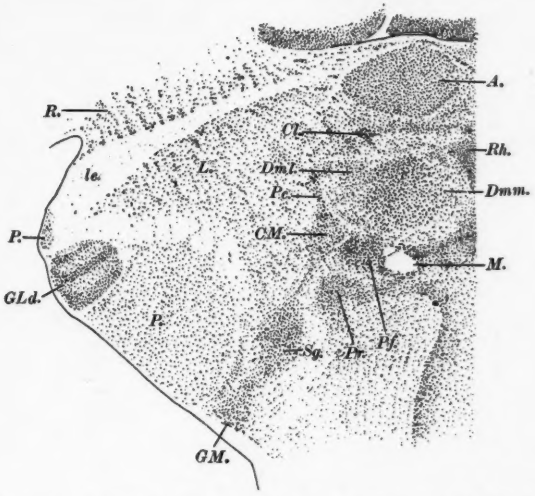


Text-fig. 14. Transverse section through medial geniculate body, pulvinar, interpeduncular ganglion, and rostral margin of pons. The section passes parallel and immediately caudal to the habenulo-peduncular tract. × 10. Iron-haematoxylin.

The comparison of the dorsal nucleus of the lateral geniculate body in *Tarsius* with other mammals in which this nucleus is at all complex involves a careful consideration of the manner and direction in which the various component laminae have become convoluted in different types, as well as the mode of entry and exit of the optic tract and cortical fibres. Such factors exhibit a very considerable variation in different orders of Mammals, and a study of them would seem to offer a promising field for taxonomic investigations. The matter is further complicated by the degree to which the whole lateral geniculate body may be displaced and rotated by the development of other parts of the thalamus. It may be noted for the present that, as far as the Primates are concerned, the dorsal nucleus of *Tarsius* approximates closely to the anthropoid type as contrasted with the Lemuroid type. Both types are evidently developed from the simple form of dorsal nucleus found in *Tupaia* (7) and the smaller Lemuroidea, such as *Chirogaleus* (15), by the expansion of the medially situated laminae, or, in other words, that part of the simpler type of dorsal nucleus which, as Brouwer has demonstrated experimentally (1), is related to binocular vision. Whereas, in the larger lemurs, this expansion has been permitted by the production of undulating folds in the medial laminae and a curving of the laminae as a whole so that they present a medio-dorsal concavity, while the optic fibres still

penetrate the nucleus largely from the ventro-lateral aspect (24), in *Tarsius* and the Anthropoidea the expansion has been obtained by an eversion of the medial laminae so that they become markedly convex medio-dorsally and extend over the lateral aspect of the nucleus, and the optic tract now enters practically entirely from the ventro-medial pole.

The lamination of the dorsal nucleus in *Tarsius* is comparable in degree with that obtaining in *Hapale* (34). The lamina superficialis corresponds to the lateral and medial strata described and figured by Woollard (though the latter are relatively thicker), while the central laminae correspond to the central



Text-fig. 15. Horizontal section through dorsal part of thalamus at the level of the anterior nucleus, dorso-medial nucleus, and upper pole of lateral geniculate body. × 10. Toluidin blue.

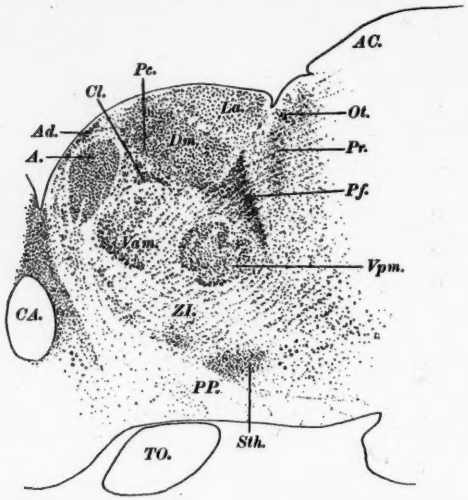
mass. There is no element in *Tarsius*, however, which can be certainly homologised with the large-celled basal laminae in *Cercopithecus* (11) and higher Primates (15). The only element which might be regarded as a pars magnocellularis, on the basis of cyto-architecture, is the group of cells on the dorso-medial aspect, to which attention has been drawn, and which appears to be a local specialisation of the peripheral lamina.

There is no distinct pregeniculate nucleus in *Tarsius*. The corpus pregeniculatum described by Woollard is evidently the rostral end of the medial portion of the peripheral lamina of the dorsal nucleus.

The optic tract (*TO.*)

The arrangement of the optic fibres in the chiasma has been described and figured by Woollard (32), from which it appears that relatively few of the optic nerve fibres pass to the homo-lateral optic tract. On the contrary, Ziehen

has stated that in the chiasma "das ungekreuzte Bündel ist ziemlich stark" (38). The relative size of the optic tract may be inferred from the accompanying figures of sagittal sections through the thalamus (text-figs. 16 to 20). The tract crosses the pes pedunculi on its way to the lateral geniculate body and, before reaching the latter, gives off the posterior accessory optic tract. This tract is conspicuous in *Tarsius*, and may be followed from the main optic tract readily enough in the sagittal sections. In the frontal section illustrated in text-fig. 13, the termination of the accessory tract in the n. opticus tegmenti is well shown. The tract contains a proportion of non-myelinated fibres. The nucleus opticus tegmenti can be recognised in toluidin blue sections as a small



Text-fig. 16. Parasagittal section close to the mid-line through anterior nucleus and nucleus parafascicularis. × 10. Toluidin blue.

group of small angular cells situated at the medial margin of the pes pedunculi and in many sections separated from the medial extremity of the substantia nigra by a clear space. However, its relation to the substantia nigra is indicated by the fact that fibres of the accessory tract can be traced beyond it into the medially placed cells of the substantia nigra itself. Conclusive experimental evidence of a positive nature has now accumulated to prove that the fibres of the posterior accessory optic tract are certainly retinal fibres (16, 17). The anterior accessory optic tract of Bochenek cannot be identified in any of the sections. If it is present, it is not distinguishable from the fibres of the supra-optic decussation of Meynert.

The relation of the optic tract to the lateral geniculate body has been described above. Towards the dorsal pole of the lateral geniculate body, the tract is considerably augmented by fibres which emerge from its dorsal nucleus,

and, further dorsally, by fibres from the pulvinar most of which have entered from the dorsal nucleus of the lateral geniculate body and have passed through the pulvinar without interruption. It is apparent, indeed, that only a small proportion of the mesencephalic root of the optic tract can be composed of fibres which have not earlier penetrated the lateral geniculate body or the pulvinar. It is probable that the optic tract dorsal to the lateral geniculate body consists largely of fibres which have originated in the dorsal nucleus of the latter. The relation of the mesencephalic root of the optic tract to the large-celled nucleus of the optic tract and to the nucleus pretectalis is described with these nuclei. The termination of the tract in the anterior colliculus offers no distinctive points for comment here.

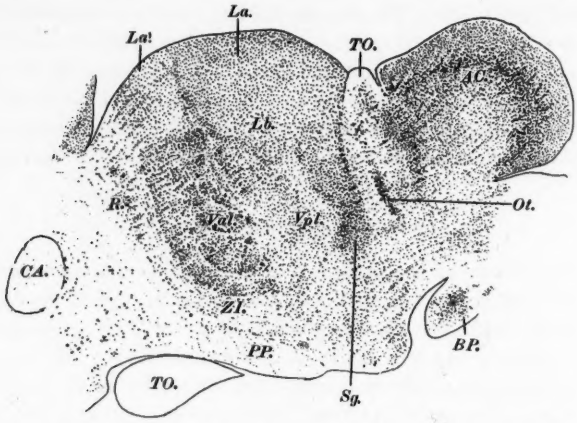
The supraoptic decussations of Ganser and Meynert are particularly distinct (text-figs. 12, 18). The former can be traced upwards and backwards and also laterally, in a curving course, skirting around the descending column of the fornix to the zona incerta, where it becomes lost in the plexus of medullated fibres which fills this area. Meynert's commissure can be traced to the ventral aspect of the pes pedunculi, and many of its fibres may be seen curving dorsally between the fibres of the crus towards the subthalamic nucleus.

Nucleus pretectalis (*Pr.*)

In my description of the thalamus of *Tupaia* (7), an account was given of a nucleus of small cells lying medio-ventral to the conspicuous group of large cells closely related to the mesencephalic root of the optic tract, and this was called the posterior nucleus of the thalamus, following the nomenclature adopted by Gurdjian in his monograph on the thalamus of the rat (12). For the same reason, the name "pretectal nucleus" was given to the large-celled nucleus of the optic tract. Attention was also drawn to the difficulties of nomenclature in this region where the thalamus abuts on the tectum. A more extensive comparative study of the thalamus of insectivores since then has led me to revise the nomenclature adopted in my previous paper. The large-celled element, which is so conspicuous a feature in the tree-shrew, has been described by Cajal in rodent material, and named by him the "Noyau de la Voie Optique" (3). Hence it seems more advisable to retain Cajal's name for this nucleus or, more conveniently, to call it the large-celled nucleus of the optic tract in order to distinguish it from Cajal's "Noyau de la Bandelette Optique," which consists of cells lying ventral to the pes pedunculi. The nucleus described as the posterior nucleus in *Tupaia*, and in the rat by Gurdjian, corresponds to Cajal's n. posterior or n. prebigeminalis, and to the n. pretectalis described by Tsai in the opossum (28). Since the term "posterior nucleus" has been applied by some authors to masses of cells entirely distinct from that originally described by Cajal, it seems advisable to use the term n. prebigeminalis or, more conveniently, n. pretectalis for this element. The pretectal nucleus, as described here for *Tarsius*, therefore, corresponds to the

element called n. posterior in *Tupaia*, while the element in the thalamus of this insectivore which was described under the name of n. pretectalis should be called the large-celled nucleus of the optic tract.

The pretectal nucleus in *Tarsius* (*Pr.*) appears in sagittal sections (text-fig. 16) as an elongated nucleus, extending ventrally and slightly caudally from the dorsal surface of the thalamus, close to the mid-line, to a point immediately caudal to the posterior limit of the ventral group of nuclei. It consists of cells of varying sizes and shapes fairly closely packed together, which show a tendency to arrangement in rows parallel to the numerous tecto-thalamic fibres which run among them. In the frontal sections stained with toluidin blue (text-figs. 7, 8) the upper end of the nucleus is first seen rostrally



Text-fig. 17. Parasagittal section through the lateral and ventral nuclei, and showing the relation of the nucleus suprageniculatus to the caudal end of the lateral nucleus. × 10. Toluidin blue.

lying medial to the posterior extremity of the main part of the lateral nucleus and the dorsal extremity of the n. suprageniculatus, and postero-dorsal to the fasciculus retroflexus and the n. parafascicularis. Dorso-laterally it is related topographically to the large-celled nucleus of the optic tract. As it becomes displaced ventrally in more caudal sections, the pretectal nucleus deviates slightly in a lateral direction, but always maintains its position relative to the n. suprageniculatus and the large-celled nucleus of the optic tract. In Weigert sections, the nucleus is seen to be filled with a very rich plexus of medullated fibres. It is traversed by numerous fibres passing between the tectum and the thalamus, many of which evidently terminate in it. It is also connected with the opposite side by fibres which cross in the posterior commissure. Ascending collaterals to the pretectal nucleus from the medial fillet have been described by Cajal. Such a connection cannot be satisfactorily determined in the available material of *Tarsius*. Vertical fibres can, however,

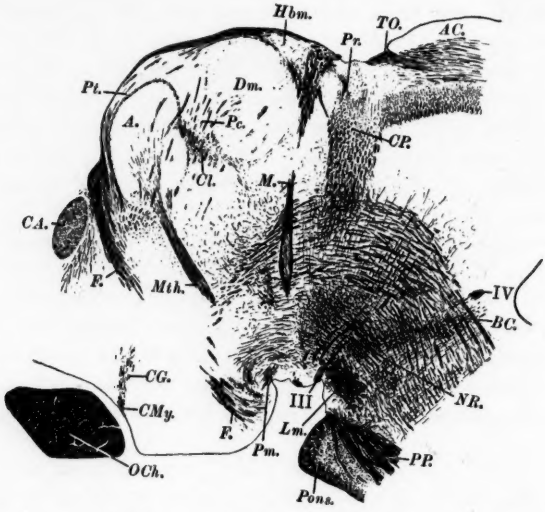
be seen running down from the pretectal nucleus to the tegmental region immediately dorsal to the substantia nigra and lateral to the red nucleus. These fibres correspond to the pretecto-tegmental tract described by Tsai (28). This author further traced some of the fibres into the substantia nigra in the opossum, forming a pretecto-nigral tract. It may be noted that in *Erinaceus* the pretecto-tegmental tract is particularly well defined and can be traced in continuity from the well-differentiated n. pretectalis of this insectivore into the tegmental region immediately overlying the substantia nigra.

Tsai (28) and Gurdjian (12), in the opossum and the rat respectively, have been able to trace optic tract fibres to their termination in the pretectal nucleus. In *Tupaia* it was not possible to demonstrate this connection conclusively, though optic tract fibres were followed in abundance up to the margin of the nucleus. In *Macroscelides*, however, in which both the optic tract and the pretectal nucleus reach a large size, the connection is clear. In *Tarsius*, the frontal sections stained with iron-haematoxylin have been cut somewhat obliquely in a ventro-caudal direction, and by a happy chance along the plane of entry of the optic tract fibres into the nucleus pretectalis. It is thus possible (text-fig. 14) to follow terminal fibres of the mesencephalic root of the optic tract through the longitudinally running cortico-tectal fibres into the pretectal nucleus, where they contribute to the medullary plexus which pervades it. There seems to be no doubt, therefore, that in *Tarsius* the n. pretectalis is a terminal station for optic tract fibres. It has been suggested (Tsai) that the pretectal nucleus in lower Mammals is the precursor of the pulvinar in Primates. The identification of the pretectal nucleus in *Tarsius*, in which also there is an element clearly corresponding to what has been called the pulvinar in higher Primates, negatives this hypothesis.

The large-celled nucleus of the optic tract (*Ot.*)

This nucleus, which, as noted above, was called the pretectal nucleus in the description of the thalamus of *Tupaia*, is a conspicuous feature at the junction of the thalamus and the mid-brain in *Tarsius*. Its position relative to the surface is indicated in the reconstruction shown in text-fig. 22 C. It consists of large cells, triangular or fusiform in shape and deeply staining with toluidin blue, which lie in the main between the upper end of the mesencephalic root of the optic tract and the coarse bundles of cortico-tectal fibres, many of them also penetrating in among the latter. In sagittal sections (text-figs. 16, 17) they form an obtrusive band of cells, closely packed together, and directed caudo-ventrally on the postero-dorsal aspect of the n. suprageniculatus. In horizontal sections, they appear as a band of characteristic cells extending postero-laterally from the postero-lateral aspect of the pretectal nucleus to the optic tract, where the sulcus indicating the junction of the thalamus with the tectum indents the surface. In this plane it lies posterior to the n. pretectalis, the n. suprageniculatus and the pulvinar in a medio-lateral direction (text-fig. 15 represents a section immediately ventral to the

level of the nucleus). In frontal sections, the nucleus first appears rostrally at the dorsal surface of the thalamus (text-fig. 7) immediately overlying the posterior extremity of the main part of the lateral nucleus and the upper end of the n. supragenicularis, reaching medially to the dorso-lateral aspect of the n. pretectalis. More caudally (text-figs. 8 to 11) the group of cells becomes flattened out into a strand which sinks in from the surface and is directed medio-ventrally between the tectum and the pulvinar. A comparison with the figures of the thalamus of *Cercopithecus* (11) and *Lemur* (24) suggests that the nucleus limitans in these forms is, in part at least, made up of cells representing the large-celled nucleus of the optic tract. Cajal (3) described

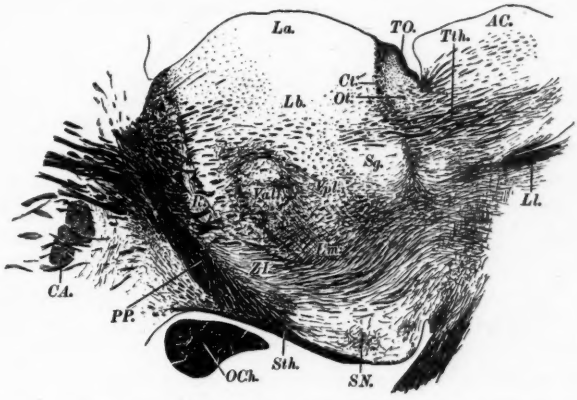


Text-fig. 18. Parasagittal section close to the mid-line. × 10. Iron-haematoxylin.

numerous collaterals running from the neighbouring optic tract fibres to the nucleus of the optic tract. Such a connection can be readily demonstrated in *Tupaia* and *Macroscelides*, in both of which insectivores the large-celled nucleus is of conspicuous size. In *Tarsius*, likewise, the iron-haematoxylin series shows (in sections immediately caudal to text-fig. 14) an abundant penetration of this nucleus by fibres from the mesencephalic root of the optic tract, many of which appear to terminate in it. Medullated fibres also leave it and pass medio-ventrally among the tecto-thalamic fibres to the deeper layers of the anterior colliculus. Cajal describes the axis cylinders of the cells as losing themselves in the white substance of the tegmentum of the mid-brain.

It is clear that, in *Tarsius*, the large-celled nucleus of the optic tract is a flat plate of cells disposed obliquely so that its superficial surface is directed laterally, rostrally and ventrally. A comparison with the equivalent nucleus

in *Tupaia* and *Macroscelides* indicates that, in *Tarsius*, it has lost its primitive superficial position (except at its rostral extremity) and has become sunk in along the junctional line between the tectum and the thalamus as the result of the expansion of the latter, especially in the region of the pulvinar. That such an "infolding" has occurred along the line of this nucleus is perhaps further evidenced by the conspicuous branches of the posterior cerebral artery, which penetrate the brain substance along the plane of the nucleus in a manner which recalls, for instance, the penetration of the lateral striate artery in a line which corresponds to the infolding of the hypopallial area of the fore-brain (10). The presence of conspicuous vessels entering the brain substance along the plane of the nucleus limitans in higher Primates is further suggestive of the conclusion that the large-celled nucleus of the optic tract becomes incorporated in the latter and thus loses its individuality.



Text-fig. 19. Parasagittal section through lateral part of thalamus. × 10. Iron-haematoxylin.

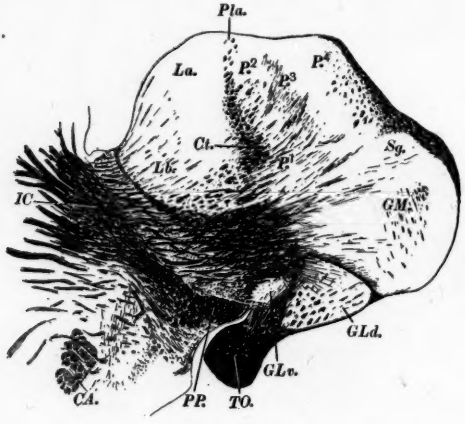
As in the case of the pretectal nucleus, the recognition of the large-celled nucleus of the optic tract in *Tarsius*, in association with a thalamic element which can certainly be homologised with the pulvinar, definitely eliminates the former as a possible precursor of the pulvinar in Primates.

It may be noted that the large-celled nucleus of the optic tract has been figured by Papez (for the cat and the sheep) under the name of "nucleus of the optic tract" or "pretectal nucleus" (23). It has also been figured by Rioch (25) (for the cat and dog) under the name of "nucleus lenticularis mesencephali." This term, however, implies homologies with the nucleus of this name in the reptilian brain which have yet to be established and, further, it is hardly appropriate to the form of the nucleus as it is found in *Tarsius*.

MEDIAL GENICULATE BODY

Corpus geniculatum mediale (*GM.*)

The medial geniculate body in *Tarsius* forms a relatively very prominent tubercle (text-figs. 1, 14). In the frontal series of toluidin blue sections it appears rostrally as a closely packed mass of small cells—oval or polygonal in shape—lying immediately medial to the caudal extremity of the lateral geniculate body, bounded dorsally by the posterior end of the pulvinar (zone 4), dorso-medially by the n. suprageniculatus, and medially by the zona incerta. More caudally (text-fig. 10) the n. suprageniculatus extends laterally between it and the pulvinar and, as has already been noted, becomes incorporated in



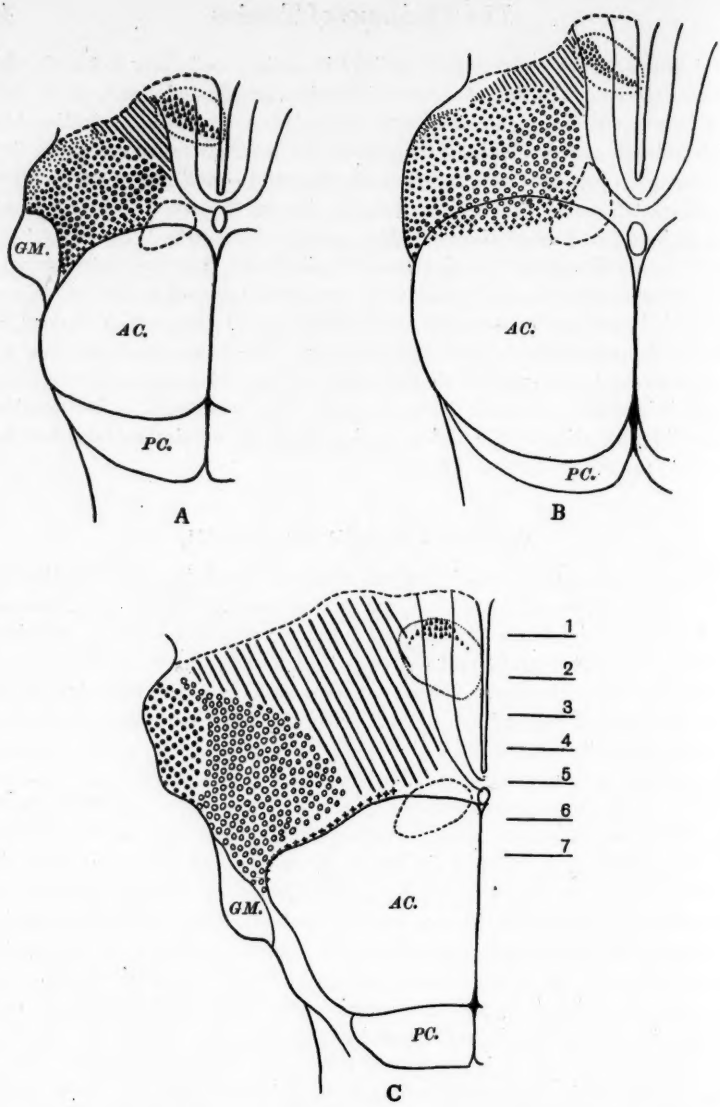
Text-fig. 20. Parasagittal section through the geniculate bodies and pulvinar. × 10. Iron-haematoxylin.

the medial geniculate body in a manner which is illustrated in text-figs. 9, 10 and 11. In the medial geniculate body of *Tarsius*, therefore, there can readily be distinguished on the basis of cyto-architecture a central mass of small cells (*GMc.*) which forms the bulk of the structure, and a dorso-lateral element, the pars lateralis (*GMl.*), consisting of larger cells, more scattered, more deeply stained, and triangular in shape, continuous rostrally, without interruption, with the n. suprageniculatus. Caudo-ventrally, the surface of the central mass is covered by a layer of cells, smaller and more darkly stained than the central element, and separated from the latter by a well-marked medullary lamina, the pars ventralis (*GMv.*). In Weigert sections (Plate II) the subdivision of the medial geniculate body is evident enough by the medullary laminae which separate the central from the marginal zones. The lateral fillet enters the medial geniculate body from the medial

aspect and appears to terminate mainly in a rich medullary network which pervades the central area. The dorso-lateral large-celled element, on the other hand, is more obviously concerned with the emission of cortical projection fibres which proceed antero-medially to pass to the internal capsule. Many fibres, however, also proceed from the central mass and contribute to the auditory radiations. The caudo-ventral small-celled element is connected by fibres with the zona incerta. A comparison with the medial geniculate body of *Cercopithecus*, as described and figured by Friedemann (11), indicates that the central group of cells corresponds to the main mass of his oro-dorsal part, while the dorso-lateral large-celled element is the equivalent of his lateral part which is very conspicuous for the size of its component cells. The caudo-ventral element in *Tarsius* seems to correspond to the caudo-ventral element in *Cercopithecus*, though it is small in *Tarsius* by comparison. It only remains to be mentioned that a differentiation of the medial geniculate body on similar lines has been described for lower Mammals (21, 30, 31).

VENTRAL GROUP OF NUCLEI

The ventral group of nuclei forms a well-demarcated element in the thalamus of *Tarsius*, both in toluidin blue and Weigert sections. In the former, the nuclei stand out as a conspicuously lobulated mass, the extent of which is sufficiently indicated by text-figs. 16 and 17. Rostrally the group extends up to the external medullary lamina by which it is separated from the reticular nucleus. Dorso-rostrally it comes into relation with the anterior nucleus and the n. centralis lateralis, while dorsally it is limited by the lateral nuclei. Caudally it is bounded by the n. parafascicularis and the pretectal nucleus, and, more laterally, by the n. supragenículatus. Ventrally, the ventral medullary lamina separates it from the zona incerta. The ventral nuclei are composed of polygonal cells of medium size, which stain relatively deeply and show a characteristic tendency to group themselves into small clusters or arrange themselves in rows that are parallel to the penetrating fasciculi of the thalamic radiations. Moreover, the whole group, as just noted, is largely split up into irregularly rounded lobules. The medial lemniscus can be traced up to its termination in the ventral nuclei, and its general course is illustrated in text-figs. 13, 14, 18, 19. The terminal fibres of this tract ascend in an antero-dorsal direction and reach the ventral nuclei on their caudo-ventral aspect. In general, they terminate in a characteristic manner by forming conspicuous capsules, which enclose and separate the several lobules of the ventral group of nuclei. From these capsules, a rich plexus penetrates into the lobules to form, within the latter, a complicated network of intertwining fibres. The ventral nuclei are thus given a distinctive appearance in Weigert sections. Although no abrupt division of the medial fillet is to be noted, there are two main terminal portions. One of these ends in the specially distinct postero-medial element of the ventral group and is shown in text-fig. 13. The other represents the main rostral



Text-fig. 21. Dorsal view of thalamus of (A) *Ptilocercus*, (B) *Tupaia*, and (C) *Tarsius*, reconstructed from serial sections. In this and the next figure, some of the thalamic nuclei have been projected on to the surface of the thalamus. ×8. Black triangles = antero-dorsal nucleus. Dotted line = main part of anterior nucleus (antero-ventral + antero-medial elements). Oblique line = main part of lateral nucleus (*La.*). Fine dots = ventral nucleus of lateral geniculate body. Coarse dots = dorsal nucleus of lateral geniculate body. Circles = pulvinar (pars posterior of lateral nucleus). Crosses = large-celled nucleus of optic tract. Interrupted line = pretectal nucleus.

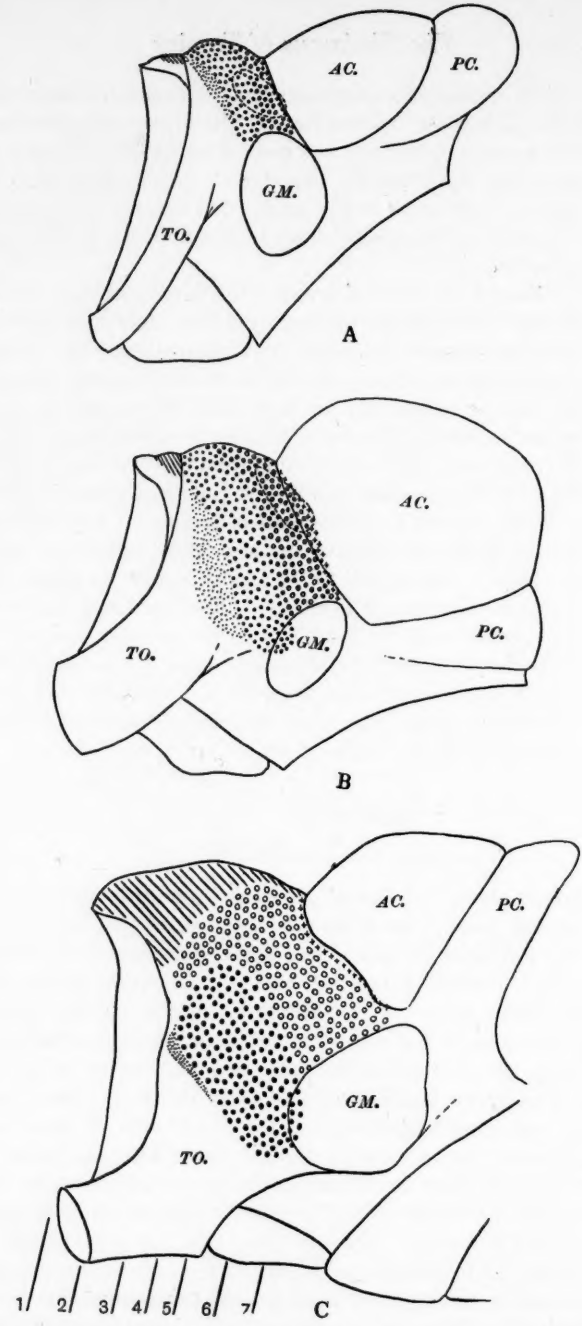
continuation of the medial fillet and is particularly associated with the antero-lateral elements. It is shown in text-fig. 19. These two main terminations of the medial fillet seem to correspond in a general way to the lateral and medial divisions of the tract described by Vogt for *Cercopithecus*, though they are not in any way so distinct as in the latter. No evidence was found of the termination of fibres of the medial fillet in thalamic nuclei other than the ventral group in *Tarsius*.

The subdivision of the ventral group into component elements is determined by the mode of termination of the medial fillet. Although these elements are not everywhere sharply delimited, it is convenient, for topographical purposes, to recognise two main parts of the ventral nuclear mass, anterior and posterior, each of which may be again divided into medial and lateral portions. The postero-medial nucleus (*Vpm.*) is the most sharply defined and, as noted above, receives a rich contribution from the fillet (text-fig. 13). It is in close relation to the fasciculus retroflexus and the parafascicular nucleus. The postero-lateral ventral nucleus (*Vpl.*) is larger but less circumscribed. It forms a relatively diffuse collection of cells lying ventral and anterior to the n. suprageniculatus and medial to the caudal half of the lateral geniculate body. The antero-medial element is relatively ill-defined and lies between the postero-medial ventral nucleus behind and the anterior nucleus in front. Laterally to it is the much larger and conspicuously lobulated antero-lateral ventral nucleus (*Val.*), from the rostral aspect of which bundles of fibres pass out into the internal capsule. It is to be emphasised that this subdivision of the ventral group of nuclei is largely of an arbitrary nature.

HABENULAR NUCLEI

Nucleus habenularis (*Hbm.*, *Hbl.*)

This nucleus shows the usual characteristic structure and relations. Medial and lateral elements are to be noted, and there is no evidence of a subdivision of the medial element into two parts as described in the rat (12) and opossum (28). The medial habenular nucleus, consisting of small, deeply stained, and closely packed cells, extends in sagittal sections from a point immediately above the dorsal pole of the subjacent anterior nucleus (separated from it here by the parataenial nucleus) back to the level of the posterior commissure. The lateral habenular nucleus has almost the same extent, but does not reach quite so far rostrally. It consists of cells of various sizes, but most of them larger than those of the medial nucleus. They are loosely arranged and triangular or fusiform in shape. Rostrally they diminish in size. Both medial and lateral habenular nuclei increase in cross-section area when traced caudally and, as the sections show (text-figs. 4–6), the lateral nucleus attains to a larger size. The formation and course of the habenulo-peduncular tract follows the common arrangement (text-fig. 18). Its termination in the inter-peduncular ganglion, however, in contrast to the usual condition, cannot be



Text-fig. 22. Lateral view of thalamus of (A) *Ptilocercus*, (B) *Tupaia*, and (C) *Tarsius*, reconstructed from serial sections. ×8 Nuclei indicated as in the previous figure.

followed in detail. The reason for this is that, while in the greater part of its course the tract consists of a central core of non-myelinated fibres surrounded by a thin sheath of myelinated fibres (Plate II), at its lower extremity it is made up entirely of non-myelinated fibres.

NUCLEI OF MID-LINE

Nucleus paraventricularis (*Pva., Pvp.*)

This nucleus consists of little more than strands of small cells disposed in vertical rows close to the median line among the periventricular fibres. These raphe cells form poorly defined groups, but condensations appear rostrally and caudally which represent the anterior and posterior paraventricular nuclei which have been described in other forms. Their relative position is indicated in text-figs. 3 and 7.

Nucleus rhomboideus (*Rh.*)

This nucleus consists of small round cells closely packed together, and forming a median group which is linked up laterally with the paracentral nucleus. In cross-section, they form a triangular mass which wedges in between the ventro-medial aspects of the dorso-medial nuclei.

Nucleus centralis medius (*Cm.*)

In some sections, through the middle of the thalamus, this median group is very conspicuous (text-fig. 5). It is formed of medium-sized deeply staining cells which link up the nucleus centralis lateralis of either side. Its cells are of the same type as those of the latter nucleus but smaller.

Nucleus reuniens (*Re.*)

This mid-line group is most evident in the rostral planes of the thalamus, lying medio-ventral to the caudal extremity of the main part of the anterior nucleus. Its cells are somewhat larger than those of the n. rhomboideus and more loosely packed.

SUMMARY

The thalamus of *Tarsius* may be said to represent the Primate type of thalamus reduced to its simplest expression within this group. While its structure is simple compared with the thalamus of higher Primates, its nuclear elements are particularly well-defined and, in their arrangement and relative development, a link is provided between the thalamus of higher Primates and that of the generalised types found among the insectivora. Thus the comparative structure of the thalamus in *Tarsius* is in consonance with the general zoological position of this animal which is, in general, the most primitive existing member of the order Primates.

Compared with the thalamus of *Tupaia* (the most progressive insectivore type from the anatomical standpoint), that of *Tarsius* is characterised by its

greater relative breadth, which is due almost entirely to the expansion of the dorsal moiety, especially that part which comprises the lateral nucleus and its appendage, the pulvinar. The lateral geniculate body is highly organised and large in so far as its dorsal nucleus is concerned. In the manner in which the laminae of this nucleus are convoluted it resembles the anthropoid type of lateral geniculate body, and shows a corresponding divergence from the lemuroid type. The ventral nucleus of the lateral geniculate body is present but relatively small. The optic tract is large and the great majority of its fibres terminate in the dorsal nucleus. The mesencephalic root of the optic tract is much smaller than in *Tupaia*, and is made up partly of retinal fibres and partly of fibres which emerge from the dorsal nucleus of the lateral geniculate body and the pulvinar. Fibres from the mesencephalic root of the optic tract partly terminate in connection with the nucleus pretectalis and the large-celled nucleus of the optic tract. The posterior accessory optic tract is conspicuous and can be observed leaving the main part of the optic tract and terminating in the nucleus opticus tegmenti.

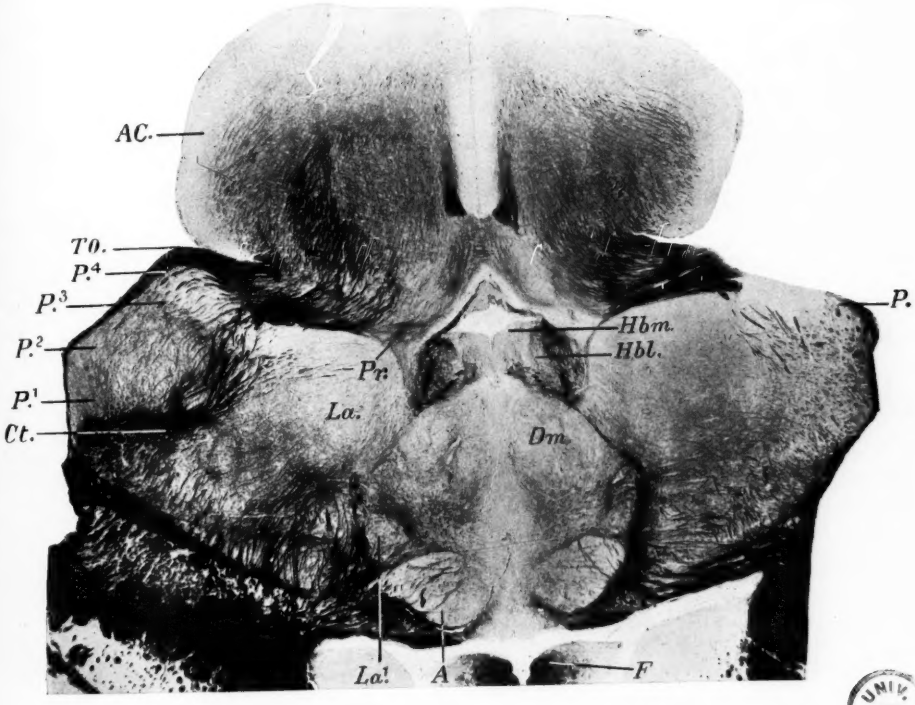
The main part of the anterior nucleus is large and particularly well-defined. Topographically it corresponds to the antero-ventral nucleus of other types, but it is suggested that it may represent also the elements which have been described under the names of antero-medial nucleus and n. submedius. The antero-dorsal nucleus is small but quite distinct.

The lateral group of nuclei is divided into a main part situated at the dorsal surface of the thalamus and which is related mainly to the ventral nuclei, and two appendages. Of the latter, one projects laterally to come into relation with the lateral geniculate body and forms the pulvinar, and the other projects caudo-ventrally as the n. suprageniculatus to reach and become incorporated in the medial geniculate body. Evidence has been adduced to show that the pulvinar of *Tarsius* is the equivalent of at least a part of what has been called the pulvinar in higher Primates and of the pars posterior of the lateral nucleus of lower forms.

The medial geniculate body forms a conspicuous nucleus in which can be discerned component elements similar to those described in higher Primates.

The ventral nuclei form characteristically lobulated masses of cells lying in relation to the termination of the fibres of the medial fillet. Compared with *Tupaia* these masses are more differentiated from each other, but the group as a whole has not undergone the relative expansion shown by the lateral nuclei.

Of the medial nuclei and the nuclei of the mid-line, attention may be drawn to the identification of the centre median nucleus. A comparison of a graded Primate-Insectivore series indicates that this nucleus, which reaches such a marked development in Man, is an elaboration of the interstitial nucleus which lies in the track of the fibres forming the caudal part of the medial medullary lamina of the thalamus. It is represented in *Tarsius* and also in insectivores.



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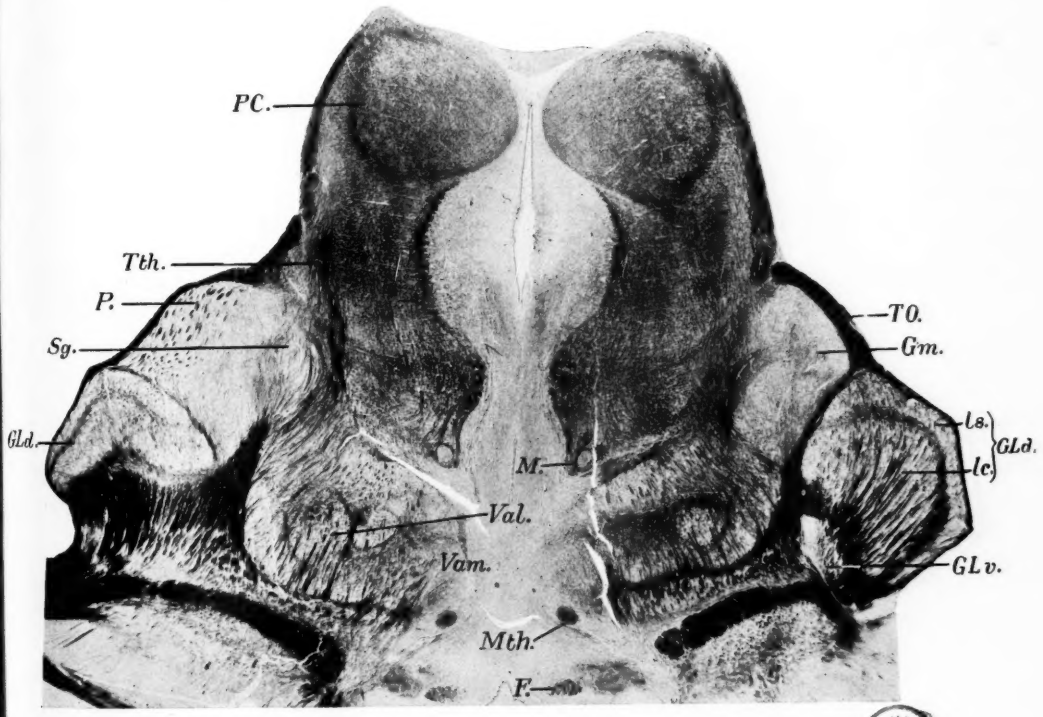

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DESCRIPTION OF PLATES I, II

PLATE I. Horizontal section at level of anterior nucleus and pulvinar. Weigert. ×12.
PLATE II. Horizontal section at level of geniculate bodies and pulvinar. Weigert. ×12.

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THE CUTANEOUS GLANDS OF MAN

By H. H. WOOLLARD
Adelaide University

It has long been known that, in addition to the usual type of sweat gland, there is a special type of cutaneous gland in the axilla which some authors have described as the "axillary organ." From investigations of the anatomy of this so-called axillary organ, a generalised conception has been evolved that there are two kinds of sweat glands, the ordinary simple tubular type or epicrine gland, and the larger compound tubular type or apocrine gland. A reading of older anatomists, such as Krause for instance, would suggest that the ceruminous glands of the external auditory meatus, the tarsal glands of the eyelid, and the circumanal glands belong to the same series as the axillary organ. In the investigation of these glands, the axillary organ has received most attention and the description that follows is based upon the morphology of the glands found there.

The introduction of the term epicrine for the simple sweat gland, and apocrine for the compound tubular, seems to be due to Schiefferdecker. Several anatomists saw the interest of determining the phylogenesis of this apocrine type, but Schiefferdecker appears to have been the first to make any attempt to use the distribution of these apocrine glands as an anthropological character.

THE APOCRINE GLAND

The apocrine gland is distinguished from the ordinary sweat gland, of which it seems to be a variety, by several features. The gland occupies the centre of the axilla and measures about 50 mm. in length, about 2 mm. in width and 3–5 mm. in thickness. While other skin glands are yellowish in colour this type can be recognised by its reddish tint. Ordinary sweat glands lie entirely within the cutis while the apocrine extend more deeply and reach as far as the subcutis.

The apocrine is a compound tubular gland and thus differs from the simple tubular type of the sweat or epicrine gland. The ducts of the glands run in close association with the hair sheaths, and in fact they are found only in regions where hair occurs. The duct may open into the cavity of the sheath, or more often reaches a depression in the epidermis close to the point where the hair issues. Homma states that apocrine glands are developed from the hair root. Where the duct joins with the secretory part of the gland there is usually an abrupt enlargement, so that point of transition can easily be recognised. The secretory units are packed close together and thus become com-

pressed at the centre of the gland but assume a more spherical shape at the periphery of the gland mass. The investing capsule is thin. Trabeculae from this split the gland into lobules. The blood supply is abundant and nerves have been followed along with the blood vessel as far as the membrana basalis. They have not been seen, however, to end on the epithelium.

The individual glands are larger than those of the simple sweat glands. The lumen measures about 0·11 mm. in diameter. The apocrine gland units resemble very closely those of the sweat glands, but the convolutions are not so marked. In the literature there has been some discussion as to whether these units undergo branching. Most observers are of the opinion that they do not branch.

FINER ANATOMY

The gland cells are bounded by a basement membrane and between the cells and the basement membrane there intervenes a layer of epithelial muscle. This muscle sheet tends to form a continuous ring within the basement membrane supporting the lining cells. The latter are one layer thick and two sorts have been distinguished. In the one case the cells are cubical and the cytoplasm is clear, while in the other the cells are a prominent columnar shape and the cytoplasm full of granules. The nucleus is situated at the centre or towards the base in both. The former type is regarded as the resting, and the latter as the actively secreting cell. The act of secretion appears to be accompanied by an accumulation of granules near the surface of the cell, the cell at this point projecting far into the lumen. The secretion appears to be actually liberated into the lumen by the rupture and fragmentation of the projecting part of the cell. Herein there seems to be another marked difference between epicrine and apocrine cells. The epicrine forms its secretion by the liberation of granules, while the apocrine actually loses a volume of protoplasm.

In the secreting cells of the apocrine gland, granules of different kinds have been seen. With osmic acid granules taking a light brown stain occur. Whether this means that they are of a fatty nature or not is uncertain, since these granules do not take the ordinary fat stains and most body elements can be made to stain in some degree with osmic acid. An intracellular yellowish pigment is also present. The apocrine cells give a positive iron reaction with Turnbull's blue method. The epicrine cells do not show this reaction. The presence of iron has been largely used by Homma as a criterion for distinguishing between the two types of glands. Our own observations, as far as they go, confirm this statement of Homma.

One other point is of interest, since a good deal depends on the distribution of these apocrine glands if they are used for racial and phylogenetic purposes. Do transition forms exist between the two? In the articles available to us the existence of transition forms is either denied or the report is cast in such a way that the problem is not raised. Nevertheless, Homma would seem to regard the transitional type as common, for he remarks there are glands still

left which cannot be certainly classified by any of the tests he enumerates. Homma draws attention to one other point which our own investigations confirm. In the post-mortem material available for such an investigation as this, fixation has been so long delayed that the material can be examined only in an imperfect condition. As the result of the late fixation, desquamation of the cells lining the lumina of these secretory glands has occurred extensively. This desquamation affects in a pronounced degree the apocrine glands, while in the same section it has not occurred in the epicrine glands. This feature, together with the size, the formation of lobules, and the iron reaction has made the identification of apocrine glands fairly obvious in some cases.

DISTRIBUTION

Brinkmann appears to have been the first to investigate the so-called axillary organ or apocrine gland in the Primates. Van Gelderen confirmed the results of Brinkmann but protested against the results obtained by von Klaar. Schiefferdecker appears to have made investigations amongst the great apes also. His results have been called in question by Brinkmann. From the literature available to us it appears as if apocrine glands were widely distributed in the lower animals. Brinkmann remarks that in orders such as the Cheiroptera and the Ungulates, skin glands of great complexity are found, while in the Primates such glands seldom occur. Von Klaar (quoted from van Gelderen), as the result of his investigations, concluded that in the lemurs all the cutaneous glands were of the apocrine type, there being no epicrine glands at all. Also in the Platyrrhines all the cutaneous glands are of the apocrine type. In the Catarrhines, however, both epicrine and apocrine are present. Among the anthropoids he found that only apocrine glands occur in the gibbon, the gorilla, and the chimpanzee, while in the orang, beside apocrine glands, epicrine glands are also present in small numbers. From this von Klaar proceeded to draw the conclusion that the orang and the Catarrhines stand more directly below Man than do the chimpanzee or the gorilla. This conclusion was attacked by van Gelderen who investigated the chimpanzee and concluded, as Brinkmann had already done, that von Klaar's results in the chimpanzee were in error, and that both epicrine and apocrine glands were present in the axilla of the chimpanzee. Brinkmann went further and determined the distribution of these two kinds of glands over the whole body in the chimpanzee and orang. He investigated skin sections taken from fifteen different regions of the body in these two anthropoids, and concludes that apocrine glands are more abundant in the orang, while epicrine are more abundant in the chimpanzee. This result is in harmony with the common views on the relationship of the various anthropoids to man.

One of the difficulties in this investigation is the influence of age. Apparently these glands are quite small and undeveloped before puberty. They enlarge and become actively secreting only when puberty is reached.

RACIAL DISTRIBUTION

Schiefferdecker studied the cutaneous glands in five German men and seven German women, a Chinese, two negroes from the Cameroons, and one Australian aboriginal. He concluded that the apocrine series of glands were especially abundant in the Chinese, less so in the African negroes and least of all in the German subjects. His material for the study of apocrine glands in the case of the Australian aboriginal was a piece of skin from the parotid region. He found the apocrine glands abundant in this, he inferred that their distribution elsewhere would be equally generous and so he concluded that the apocrine glands were most abundant of all in the Australian aboriginal.

On the basis of the frequency of the apocrine glands he suggested a hierarchy beginning with the Mammals generally, and followed by the Primates, the Australian aboriginal, the Chinese, the Cameroon negroes, the German women and finally the German men. Schiefferdecker, of course, realises that these glands are subserving some physiological purpose and that functional needs will play a part in determining their frequency and distribution.

Homma examined some eleven white subjects and twelve American negroes in Baltimore, U.S.A. He concluded from sections taken from the various parts of the body that the apocrine glands were three times more common in the negroes than in the whites and that in both races they were more common in women than in men.

THE PRESENT INVESTIGATION

Two bodies of mature aboriginal males became available in this department and the opportunity of investigating the cutaneous glands was taken. Large strips of skin were removed from these formalinised bodies. They were taken from the axilla, the mammary region, the pubic and the circumanal region. They were embedded in celloidin and cut in series at 25μ. Some sections were stained with haematoxylin and van Gieson, and every tenth section was stained according to Turnbull's blue method and counter-stained in paracarmine.

In general it may be said that large compound tubular glands of the apocrine type, as well as epicrine glands, were found abundantly in the axilla and in the circumanal region in both cases. In the other regions there were found no clean-cut cases of apocrine glands, though several were recorded as doubtful. A difficulty in interpretation arises here. The observers who described the apocrine glands of the axilla, the so-called axillary organ, were dealing with a large gland several centimetres in length, and if this is the type of apocrine gland then such a description is only applicable in the present instance to the cutaneous glands of the axillary and anal region. It would appear from the paper of Homma that he has applied the term to glands which are not of this large compound nature, but rather to glands somewhat larger perhaps than the simple tubular gland, with desquamated epithelium, and giving the iron

reaction. Moreover, he has included, judging from his results, glands as apocrine in which the iron reaction was absent.

A brief account of the several regions studied is as follows: In the axilla large lobulated apocrine glands are present. In the sections they are very apparent and the ducts can be followed alongside the hair sheath, and where the opening is seen it appears to be placed adjacent to the exit of the hair. Again their extension beyond the cutis into the subcutis is seen and also the fibrous investment. The iron reaction is positive. The axillary organ is similar in the two cases examined.

Krause has described anal glands as occurring about 15 mm. from the anal margin where they form an oval ring of about the same width. The individual glands are about three times the size of those in the case of simple sweat glands. The gland mass has a strongly developed adventitia and muscularis.

It is apparently these glands that have been observed in the sections of the circumanal region of the two aboriginal males. In such sections gland lobes of considerable size have been encountered extending throughout sections 2·5 cm. wide. The lobes are the same size as those described forming the axillary organ. The resemblance is not confined to that of size, but the individual glands are of the same dimensions and their lumina are filled with coagulated material and desquamated cells. Moreover, they react with the same intensity to the iron stain, blue granules occurring in the cells and in the lumina. One might speak of an anal organ as others have spoken of an axillary organ.

These glands, then, are in every way identical with those special apocrine glands found in the axilla, and at first it was considered that they might form a series of glands in the anal region peculiar to the Australian aboriginal. On reflection, however, this seems improbable, and it is more likely that these are nothing else than the glands described and referred to as the circumanal glands in all the standard text-books of anatomy (Cunningham, for instance). The former idea was aroused by the results obtained by Homma in the study of the circumanal skin of 11 whites at Baltimore. In this series, which included both males and females, a study of the sections of the area in question revealed apocrine glands only in 9 out of a total of 129 sections examined. From this it must be concluded either that such glands as we have met in the aboriginal do not occur in whites in Baltimore, or that they have been missed. In view of the precise description given by Krause and repeated by later anatomists, it is concluded that Homma missed them in the whites.

In the study of 179 circumanal sections from 12 negroes of both sexes, Homma states that he saw apocrine glands in 96 sections. He makes no remark on their abundance in individual sections and does not discuss their similarity with the axillary glands. He speaks of the axillary glands as densely arranged so that many of them can be examined in a single section. In the opening lines of his paper he refers to the apocrine glands of the anal region as being widely scattered.

In the mammary region the total number of sections examined in the present series was 104. Of these, 57 from one subject showed an apocrine gland once, while in the 47 from the other subject 8 were regarded as possible apocrine glands. Homma found none in 139 sections from whites and 6 in 120 sections from negroes. The apocrine glands from this region (the same applies to the pubic region) are totally unlike the massive series met with in the axilla or the anal region. Occasionally a group of glands is met with in which the lumen is slightly larger than in the case of the simple glands. In such glands the lumen may be filled with coagulated material and desquamated cells. In some cases they give a positive iron reaction. Furthermore, glands have been encountered which are clearly part of a complex of simple sweat glands, belonging to the same duct and invested by the same sheath, but are distinguished by a positive iron reaction from the rest of the gland mass. All these have been counted as examples of apocrine glands, but nevertheless some hesitation was felt in doing so. The slightly greater frequency in the Australian aboriginal of apocrine glands in the mammary region does not seem very significant. In addition to the difficulties of deciding what should be called an apocrine gland, sections taken at random from what is vaguely called the mammary region, and moreover sections unequal in area, are likely to give results which could only have value when the differences were either very great morphologically or numerically.

It is presumed that what Homma calls the mons veneris region is the equivalent of the pubic region in the males. The remarks made on the apocrine glands in the mammary region apply equally to this region. Homma's results give a percentage of 31·5 per cent. in the whites, 65 per cent. in the negroes; my own in the Australian aboriginals, 12 per cent. based on 104 sections. The comments made on the significance of these numbers in the mammary region are applicable also in the pubic region. Even if they are regarded as significant they do not arrange the races mentioned in an order which corresponds to that implied in the term primitive.

In general I would conclude that an analysis of the relative proportions of the apocrine and epicrine glands in existing varieties of man would furnish an anthropological character of very doubtful value. In fact, from my present experience I would say that it does not present a character of any anthropological value and that the Australian aboriginal has much the same variety and distribution of cutaneous glands as appears to be found in European races.

SUMMARY

1. An attempt, following on the work of Homma and others, has been made to analyse the frequency with which apocrine and epicrine glands occur in the skin of the Australian aboriginal.

2. The percentage of apocrine glands in the mammary and pubic regions show variations whose directions do not mutually accord.

3. The method used has too many sources of error to make the numerical values of much importance. In the pubic region, where the differences are greatest, the racial order so derived would advance the Australian aboriginals in front of the whites.

4. The large circumanal glands in Australian aboriginals are regarded as the equivalent of the circumanal glands of European anatomy.

5. If circumanal glands are few and scattered in the white and if they are of the same type though more frequent in the negro, then the large circumanal glands of the Australian aboriginal may be a character of some racial importance. This latter conclusion is rejected.

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THE OVARY OF *ORNITHORHYNCHUS*, WITH SPECIAL REFERENCE TO FOLLICULAR ATRESIA

By MARY LEE GARDE, B.Sc.
Lecturer in Histology and Embryology, University of Sydney

INTRODUCTION

The material studied in this paper is part of the collection of *Ornithorhynchi* accumulated by the late Prof. Launcelot Harrison, who, before his death, very kindly made over the genital tracts and ovaries for the purpose of this investigation. The entire collection has been entrusted to the Department of Anatomy in the University of Sydney, as a memorial gift by Mrs Harrison. The material is of unique value not only on account of the impending extinction of *Ornithorhynchus*, but also because of the years of careful observation and patience expended in collecting. Other *Platypus* material is in the possession of Prof. J. P. Hill, who, in collaboration with Prof. J. B. Gatenby (37), published in 1926 a description of the monotreme ovary, with particular reference to the corpus luteum. Because of the rarity of *Platypus* it was deemed advisable to embody in this work a further full description of the corpus luteum, a procedure, however, which merely serves to confirm and amplify the work of Hill and Gatenby. In the main this paper deals in detail with the histology of follicular atresia. Apart from Gatenby and Hill, no recent contributions have been made to the study of the monotreme ovary; the work of Owen, Poulton and Caldwell will be referred to in the text; other early workers in this field are Guldberg (30) and Beddard (3), 1885, and Semon (67), 1894.

BREEDING HABITS

The breeding season of *Ornithorhynchus* occurs in August and September in New South Wales.

At fertilisation the spherical ovum has a diameter not exceeding 4·5 mm. The egg increases in size by imbibition of fluid from the actively secreting glands of the uterine mucosa, and acquires a coat of albumen and a shell during its intra-uterine passage: finally at laying it is ellipsoidal, with a diameter of 16–18 × 14–15 mm. Two is the usual number of eggs laid, but instances of one and three are recorded. Normally, oviposition takes place during late August and early September. After laying, the eggs are incubated in the nesting burrow by the mother, for an unknown period; Burrell (8) suggests fourteen days as the duration of incubation. There is no activity of the mammary glands at hatching, and it is thought that lactation does not commence

until at least three weeks later. Large young are found in the nests from the later part of September to the end of October.

REPRODUCTIVE ORGANS

In the *Platypus* the left ovary and oviduct alone are functional. The average functional ovary measures 1·5 cm. in length by 1 cm. in thickness; the non-functional ovary varies in its development, but always is much smaller. The anterior end of the Fallopian tube communicates with the coelom by a large ostium, which, specially after ovulation, is closely applied to the ovary, thus concealing the large follicles projecting upon its surface. The narrow convoluted Fallopian tube passes insensibly into the uterus, the distal enlarged region of the oviduct. Posteriorly each uterus opens separately into the urogenital sinus, which discharges its contents into the cloaca. The right oviduct is not generally as well developed as the left, nor has the Fallopian tube been seen in close contact with the non-functional ovary. The glandular uterine mucosa becomes considerably enlarged during the passage of the ova down the oviduct. In the resting condition it has an average thickness of 0·55 mm. in both functional and non-functional sides. The uteri containing segmenting ova of approximately 5 mm. have a mucosa approximately 3 mm. thick, while that of corresponding non-functional uteri is approximately 2 mm. The uterus containing 8 mm. ova is slightly less than the former cases. In a *Platypus* with a late corpus luteum, the mucosa is apparently undergoing regression, and has a thickness of 1·66 mm. in the functional, and a little less in the non-functional uterus.

The general plan of the reproductive organs of *Echidna* is similar to that of the *Platypus*, but both sides are functional. Posterior to the Fallopian tube, the oviduct is differentiated into an anterior stenosed and a posterior dilated region.

MATERIAL

The following are the chief features of the functional uteri and ovaries:

P. II. No data of collection. Uterine mucosa approximately 1·6 mm. thick. One corpus luteum in an advanced state of development. Several large normal follicles. Several medium-sized blood follicles. Two large follicles recently ruptured internally.

P. III. Collected in New England, New South Wales. 9. x. 23. Uterine mucosa in resting condition, 0·6 mm. thick. Absorption of small ova. Extensive haemorrhage in large follicles, some being absorbed *in situ* and others opening internally. Two pigmented bodies formerly open externally.

P. IV. Collected at Manilla, New South Wales. 10. x. 23. Uterine mucosa in resting condition, 0·55 mm. thick. No large normal follicles. Several large follicles with extensive haemorrhage both absorbed *in situ* and open internally. Two pigmented bodies formerly open externally.

P. V. Collected in New England, New South Wales. 9. x. 23. Uterine

mucosa enlarged, approximately 3 mm. thick. Left uterus containing two ova measuring 5·0 and 5·5 mm. in diameter (Burrell states that mammary glands were quite dry, but records "an inflamed condition of the uterus"). Three corpora lutea. No large normal follicles, a large number of small and a few medium normal follicles. Later stages of absorption of many small follicles. Three large follicles open internally. No blood follicles of either type. One large follicle ruptured externally. Two pigmented bodies formerly open externally.

P. VI. Collected at Manilla, New South Wales. 20. IX. 20. Condition of uterine mucosa similar to *P. V.* Left uterus containing two ova approximately 4·5 and 5 mm. in diameter. Two corpora lutea. Absorption of smaller follicles. One large follicle recently ruptured internally. One follicle ruptured externally. Later stages of many follicles ruptured internally.

P. VII. No data of collection. Uterine mucosa evidently undergoing regression, of less diameter than the two preceding. Left uterus containing two ova of approximately 8 mm. diameter. Two corpora lutea. Absorption of many small follicles. A number of small follicles ruptured internally.

Echidna. Collected at Eidsvold, Queensland. 4. IV. 24. Uterine mucosa in resting condition, approximately 0·75 mm. thick in lower region. Several large normal follicles. In one ovary three large follicles ruptured internally with extensive haemorrhage.

TECHNIQUE

All tissues were fixed in Bles fluid in the field.

In most cases the ovaries were embedded in celloidin and paraffin. In *P. VI* the Fallopian tube was dissected away from the ovary, the corpora lutea removed and sectioned separately, one transversely and the other longitudinally. The remainder of this ovary and the complete ovary of *P. VII* were prepared by the Legroine paraffin method. The non-functional ovaries were embedded in paraffin. All ovaries were cut serially and sections were made of various regions of the uteri. Haematoxylin and eosin were used for staining.

1. General structure of the monotreme ovary

The ovary is oval to triangular in transverse section, with a distinct hilum at the attachment of the mesovarium. Externally it is covered by a layer of epithelium, whose cells vary from a flattened to a columnar form. The follicles are confined to a peripheral cortical region, where the stroma is more dense. There is no trace of oogenesis in any of the ovaries examined.

(*a*) In the functional ovary the smallest follicles and those nearing maturity tend to be external, the latter projecting markedly on the surface. The largest ova observed measure approximately 3 mm. in diameter. The stroma of the medulla is in the form of trabeculae carrying blood vessels, and lacunae in

which are phagocytic cells and masses of yolk in varying phases of degeneration. This is a characteristic feature of the functional ovary of Monotremes and is due to a peculiar method of follicular atresia.

(*b*) In the smaller non-functional ovary, the ova never reach maturity but undergo atresia at different stages of development. The largest normal ovum observed has a diameter of 1·3 mm. The medullary region consists mainly of fibrous tissue. The lacunae do not form such a marked feature as in the functional ovary.

2. Histologically normal follicles

The follicles are of the sauropsid type. The ovum with its excentrically placed nucleus completely fills the follicle, and the follicular epithelium remains a single layer throughout its development. The ovum is invested by a homogeneous membrane, the zona pellucida, in all but earliest stages. Externally the stroma is modified to form the theca, which later is differentiated into a more cellular theca interna, and a more fibrous theca externa. There is no sharp line of demarcation between the theca interna, theca externa and general stroma.

(*a*) In the smallest follicles, the ova, whose cytoplasm appears finely granular, have a diameter of 0·08 mm. and are not invested by a zona pellucida (Plate I, fig. 1). The follicle epithelium consists of a single layer of flattened cells; the theca is a thin coat showing a concentric arrangment of fibroblasts.

(*b*) Yolk granules appear in the cytoplasm of ova measuring 0·37 to 0·4 mm. in diameter (Plate I, fig. 2). There is a peripheral region of yolk-free cytoplasm which surrounds the excentric nucleus and is continued as a core to the centre of the ovum. The zona pellucida appears as a thin homogeneous layer enveloping the egg cell. A single layer of cubical cells constitutes the follicle epithelium; the theca is similar to that of the preceding stage.

(*c*) In the ovum of 0·4 to 0·5 mm. in diameter the zona pellucida attains the maximum thickness of approximately 0·008 mm. The yolk granules are more developed and show the same distribution as group (*b*). The follicle epithelium is a single layer of cubical cells somewhat irregularly arranged. The cells of the innermost part of the theca tend to be polyhedral, while those externally retain the elongated form (Plate I, fig. 3); thus the differentiation of the theca is just beginning. In some ova of this stage a conspicuous feature is the "zona radiata," a radially striated structure, less deeply staining than the zona pellucida, and placed internal to it (Plate I, figs. 2, 3).

(*d*) In this material the diameter of the largest ovum does not exceed 3 mm., and there is no indication of maturation spindles or polar bodies. The distribution of the yolk globules is similar to that of the Bird. The zona pellucida is thinner, of approximately 0·002 to 0·003 mm. in thickness (Plate I, fig. 4). The follicle epithelium is a single layer of subcubical cells upon a membrana propria. The cells of the theca interna are polyhedral, with transition stages to the flattened elongated forms of the more fibrous theca externa.

3. Corpus luteum

The most recent corpora lutea are found in ovary ***P. V*** (Plate II, fig. 1); there still remains a small central cavity upon which the luteal cells are encroaching, and the thecal ingrowths are well marked. In the next stage, ***P. VI***, the luteal cells have advanced further, almost completely obliterating the cavity; vacuolation of the luteal cells, both in the cytoplasm and in the nuclei, is more conspicuous (Plate II, fig. 2). Ovary ***P. VII*** contains two fully formed corpora lutea; compact vascular bodies whose luteal cells show regressive changes (Plate II, fig. 3). In ovary ***P. II*** there is a corpus luteum in a late stage of regression, consisting mainly of fibrous tissue, in which are scattered degenerate luteal cells (Plate II, fig. 4).

(*a*) ***Ovary P. V.*** Two ova, 5 and 5·5 mm., are present in the left uterus and the corresponding ovary contains three corpora lutea, two of which are more or less spherical, with diameters of 2·75 × 2·5 mm., and 2·96 × 2·24 mm. The luteal tissue (including ingrowths of theca interna cells) measures 2·32 × 2·24 and 2·88 × 1·92 mm. respectively in its greatest diameters. The third corpus luteum is elongated, the entire diameter being 3·04 × 1·6 mm., and that of the luteal tissue 2·9 × 0·88 mm. All three corpora lutea are similar in structure. In macroscopic view the corpora lutea project among the larger ova upon the surface of the ovary. They are of a larger size than the ova, and are flask-shaped bodies with a circular point of rupture forming the most prominent portion of the corpus luteum. In the preserved state they show the same coloration as the remainder of the ovary. The lobulation of the corpus luteum is associated with the trabeculae of thecal ingrowth among the masses of luteal cells. The latter are encroaching upon, but have not yet completely filled, the central fibrin cavity. At the site of the rupture an epithelial plug (*bouchon épithélial*) is formed, where the luteal cells project upon the surface of the ovary. Here the lips of the luteal tissue have not yet fused, with the result that the central cavity is still in communication with the exterior. The outermost coat of the corpus luteum is composed of the theca externa, consisting of fibroblasts and fibres concentrically arranged; from it arise offshoots of fibrous tissue, of which six or seven are seen in transverse section, penetrating between groups of luteal cells (Plate II, fig. 1).

Forming an irregular layer internal to the fibrous tissue are cells of a larger size with deeply staining oval nuclei, which are usually referred to as theca interna cells, in contradistinction to the typical fibroblasts of the theca externa. At the apices of the fibrous ingrowths the theca interna cells are most conspicuous, they also penetrate between individual luteal cells as far as the central cavity, where they assume a more elongated form, and are even found occasionally in the central fibrin (Plate III, fig. 1). Transition stages are observed between the typical fibroblasts and these more mobilised theca interna cells.

In the outer region of the theca are the larger blood vessels whose branches enter the luteal tissue at all points at the periphery, more especially in the

thecal ingrowths (Plate II, fig. 1). Capillaries penetrate between the luteal cells, attaining their greatest development in the epithelial plug. The luteal cells, elongated and tapering, are loosely approximated one to the other, especially in the central region (Plate III, fig. 1). They have an average size of 0·058 × 0·029 mm. and their nuclei, which are spherical or oval, vary from 0·02 to 0·025 mm. Nuclear vacuolation is seen occasionally, and less frequently the finely granular cytoplasm is vacuolated. Isolated patches of fibrin occur near the periphery of the luteal tissue, apparently representing local extravasations. The central cavity contains fibrin and occasional masses of degenerating red corpuscles; the numerous polymorphonuclear leucocytes are apparently associated with the organisation of fibrin rather than with the degeneration of luteal cells (Plate III, fig. 1). In the fibrin network are found small homogeneous globules of varying size, inter-cellular in position.

In one corpus luteum, where the central cavity remains in communication with the exterior, a fibrin mass invaded by fibroblasts, and surrounded by red blood cells, is situated in the aperture of the plug region; on the surface of the ovary, associated with each corpus luteum, are degenerate blood corpuscles and fibrin. In another corpus luteum the luteal cells of the plug are covered by two or three layers of fibroblasts continuous with those of the theca.

(*b*) *Ovary P. VI.* The ovary contains two corpora lutea, and there are two intra-uterine ova approximately 4·5 and 5 mm. in diameter. In transverse section one corpus luteum has a diameter of 2·88 × 2·32 mm., with luteal tissue measuring 2·24 × 1·6 mm. The other corpus luteum in longitudinal section is 2·48 × 1·84 mm. with luteal tissue 2·32 × 1·04 mm. Both corpora lutea are similar in structure. Although the intra-uterine ova of this specimen are smaller than those of the preceding, the corpora lutea are further developed. The cavity is almost obliterated by luteal cells, which for the most part meet in the centre of the follicle. Peripherally the luteal tissue is more compact, but the central cells retain their tapering form with well-marked cell boundaries. In the theca externa are large blood vessels. The fibrous coria of the thecal ingrowths are smaller, and the groups of theca interna cells less conspicuous, owing to a decrease in both size and number (Plate III, fig. 2). At the same time areas of lightly stained fibrous tissue make their appearance between groups of theca interna cells, and extend towards the central region, evidently the first indication of the core found in the later corpora lutea. The network of the fibroblasts and capillaries is more developed than in the preceding phase.

The luteal cells have average dimensions of 0·0624 × 0·025 mm. The largest attain a size of 0·075 × 0·021 mm., while those situated peripherally, of more spherical form, measure approximately 0·0416 × 0·0376 mm.; the majority of the nuclei are smaller. Many cells possess in their cytoplasm large spherical vacuoles, juxtanuclear in position. In other cells nuclear vacuolation has occurred, but is no more frequent than in the previous stage.

Leucocytes are more numerous in the fibrin of the reduced central cavity and neighbouring inter-cellular spaces. The small spheres are seen less frequently in the cavity. In these corpora lutea, the luteal cells spread in a lip over the theca externa in the plug region, forming a prominent *bouchon épithélial*. The capillary network of this tissue is remarkable in its great increase, being almost equal in area to that of the luteal cells. Fibrin, in a process of organisation by fibroblasts, covers in part the epithelial plug (where it is continuous with the fibrous tissue core) and extends over about one-half of the corpus luteum in a layer of average thickness of 0·146 mm.

(*c*) *Ovary P. VII.* Two corpora lutea are present in the ovary, and the two intra-uterine ova measure approximately 8 mm. in diameter. The maximum diameter of one entire corpus luteum is 2·88 × 2·83 mm., and the luteal tissue 2·56 × 2·24 mm. The greatest dimensions of the other corpus luteum are 3 × 2·56 mm. and the luteal tissue 2·8 × 2·24 mm. The corpus luteum is a completely solid structure in which the luteal cells are characterised by various forms of degeneration, and are supported by a well-developed connective tissue framework and a complex capillary system, the whole being surrounded by theca externa (Plate III, fig. 3). The thecal ingrowths typical of earlier corpora lutea are absent as definite projections, being represented only here and there by large groups of theca interna cells. The fibrous tissue reaches its greatest development at the periphery of the luteal tissue and forms a well-defined central core of the corpus luteum (Plate III, fig. 4).

The maximum diameter of the luteal cells is 0·065 × 0·054 mm., but the majority are smaller; each cell is outlined and separated from its neighbours by fibroblasts and large capillaries (Plate III, fig. 3). Most nuclei are pyknotic, and all stages of nuclear vacuolation are observed; those nuclei not vacuolated possess a crenated nuclear membrane and contain two or three small homogeneous non-chromatin spheres. Late stages of vacuolation are represented by a nuclear membrane, to which is applied the remains of nuclear substance, surrounding a spherical vacuole. Some nuclei may attain the dimensions of previous stages (0·0208 mm.), and while a few vacuolated ones are considerably larger (Plate III, fig. 4) the majority are smaller. The cytoplasm of a few cells shows vacuoles whose contents are unstained or absent, as in earlier stages; many cytoplasmic vacuoles contain a more or less spherical mass (granular sphere) in which are coarse as well as fine granules (Plate III, fig. 3). Very rarely in other vacuoles there occur several homogeneous globules of varying size, or a single larger globule, in appearance similar to those in the fibrin of the central cavity of early corpora lutea.

Leucocytic invasion of the luteal tissue is a marked feature of this stage of the corpus luteum. Polymorphs are present in great numbers in the fibrous tissue and capillaries, in the cytoplasm of degenerating luteal cells and even in nuclei in late stages of regression (Plate III, fig. 4). The luteal cells of the epithelial plug are covered by the remains of a fibrin mass, thickly invaded by the neighbouring theca cells, with which the fibrous central core is

continuous, at the site of rupture (Plate II, fig. 3). The fibrin attains a maximum thickness of 0·12 mm. and spreads over the surface of the corpus luteum as a thin lamina.

(*d*) *Ovary P. II.* The ovary contains one corpus luteum, but there is no intra-uterine ovum, or record of egg or young. The entire corpus luteum measures 2·08 × 1·44 mm. in diameter and the luteal tissue 1·76 × 0·96 mm. The luteal tissue of this corpus luteum, which is in an advanced state of regression, has been replaced by a dense fibrous tissue, in which are isolated degenerate luteal cells (Plate II, fig. 4). Internal to the thickened theca externa are small groups of theca interna cells, whose deeply staining oval nuclei form the most conspicuous feature of this stage (Plate IV, fig. 1). Certain characteristics of the previous phase are seen in the luteal cells; most frequently are found pyknotic nuclei, while occasional nuclei show vacuolation (Plate IV, fig. 2). Numerous granular spheres, in which the larger granules predominate, are situated in cytoplasmic vacuoles (Plate IV, fig. 2). Polymorphs are less prevalent than in the previous stage. The corpus luteum is no longer a copiously vascular body; the blood vessels of the theca interna cells are less numerous and thick walled (Plate IV, fig. 1). The capillaries of the central region are also less abundant and of smaller diameter (Plate IV, fig. 2). Fibrin masses remain in the thecal tissue in the region of rupture and partly covering the free surface of the corpus luteum (Plate II, fig. 4).

4. Atresia

In the ovaries under discussion follicular atresia is the frequent fate of the ovarian follicles. Atresia appears to supervene at all stages of development of the ovum; while the mechanism of destruction varies in its method, a constant factor is the phagocytic rôle of the follicle epithelium.

Ova are absorbed *in situ* by phagocytic epithelial cells; others undergo atresia by a process wherein the follicular wall ruptures and the contents pass either internally into lacunae of the medullary region, or externally upon the surface of the ovary. Each of the main processes has been described under two main headings—the atresia of small follicles prior to or during the early stages of yolk formation in the ovum, and that of large follicles containing heavily yolked ova.

A. *Absorption* in situ

This process overtakes follicles in both functional and non-functional ovaries. Three methods of absorption *in situ* have been observed:

(*a*) The absorption of small follicles containing ova with little or no yolk.

(*b*) The absorption of large follicles containing heavily yolked ova.

(*c*) The absorption of large follicles, in which a haemorrhage from the thecal blood vessels escapes into the heavily yolked ovum.

Intermediate types occur between (*a*) and (*b*) in those ova which represent transition stages of growth.

(*a*) *Absorption of small follicles* prior to and during the first stages of yolk formation in the ovum.

The largest ova in follicles of this type attain a diameter of approximately 4·4 mm. The first apparent changes occur in the cytoplasm, the nucleus, and the zona pellucida. The follicle loses its spherical form and is often oval in transverse section. The cytoplasm stains more densely and has a vacuolated appearance, perhaps due to the loss of deutoplasm in preparation.

In the majority of ova, the nuclear membrane and chromatin has disintegrated and undergone solution and the site of the nucleus is represented by a denser yolk-free area of cytoplasm. The zona pellucida increases in thickness to 0·01–0·016 mm., but always retains the homogeneous appearance and staining reaction exhibited in normal ova. A characteristic feature is the manner in which the follicular epithelium, which becomes two-layered peripherally, sends ingrowths beneath the thickened zona pellucida into the degenerating ovum. The theca shows no differentiation into internal and external layers (Plate IV, fig. 3).

In the subsequent stages the epithelial ingrowths increase in size and number, with progressive complicated folding and massing of the zona pellucida. At the same time the cytoplasm is reduced in quantity, and becomes yet more deeply staining. In a transverse section through the centre of the follicle, more than half the contents are epithelial masses capped by zona pellucida, the ingrowths being continuous with the peripheral epithelial layer. Cells of the follicular epithelium, both peripherally and in its internal folds, become mobilised and pass through the zona pellucida to reach the degenerate egg cytoplasm. Thus are formed the typical phagocytes associated with early stages of all types of atresia. These new cells acquire cytoplasmic increments and show a diminished affinity for acid stains (Plate IV, fig. 4). As the follicle is gradually reduced in size, the peripheral epithelium again becomes a single layer; cell division has not been observed at any stage. The egg cytoplasm is absorbed by phagocytes which early degenerate, while at the same time the folding and invasion of the zona pellucida becomes more complex (Plate V, fig. 1). The degree of folding of the zona pellucida varies. In some cases it remains an almost uninterrupted sinuous layer surrounded by and enclosing epithelial cells (Plate V, fig. 3). In others where the zona has become invaginated as far as the central region of the ovum, it later appears as a reformed peripheral lamina with scattered fragments among the inner mass of cells (Plate V, fig. 2). The peripheral epithelium eventually disappears and the follicle is represented by areas of fragmented zona, sown with cells, surrounded by a contracted fibrous capsule, the theca (Plate V, fig. 4). The included cells degenerate, and small patches of zona are found scattered in the theca. The last stages of the follicle are obliterated by absorption of the disintegrated zona pellucida and growth of the theca.

It is to be noted that the follicles undergoing this type of atresia have reached the stage of development where the zona pellucida attains its maximum thickness.

(*b*) *Absorption of large follicles* containing ova in which yolk formation has occurred.

In these follicles, many of which lose their spherical form, the largest ovum has a diameter of 1·3 mm. in the functional, and of 0·65 mm. in the non-functional ovary. In early stages, the ovular cytoplasm stains deeply with haematoxylin, while the yolk globules take the eosin stain more readily than in normal ova. The zona pellucida is often somewhat thicker than in normal follicles of the same size. The follicle epithelium consists of two or more irregular layers. The inner region of the theca of many follicles shows increased vascularity, and is generally more cellular than the outer part (Plate V, fig. 5). The epithelial cells invade the zona pellucida, which rapidly loses the thick homogeneous appearance characteristic of the smaller atretic follicles, and in the preparations is shrunken away from the invading cells (Plate V, fig. 6) which penetrate to the peripheral cytoplasm between the yolk globules, assuming the phagocytic form. At the same time the external epithelium is reduced to a single layer of cells (Plate VI, fig. 1). At a later stage the limiting single-layered epithelium disappears, and the fragmented zona pellucida comes to lie in contact with the adjacent theca (Plate VI, fig. 2).

The next phase of atresia is associated with changes in the yolk globules, changes which differ according to the yolk content. In those follicles in which yolk is not abundant, the spheres are ingested directly by phagocytes (Plate VI, fig. 2). In the more heavily yolk-laden follicles there is a peripheral invasion and ingestion of the yolk globules, but the invasion of the central areas is delayed, the yolk deposits coalescing to form large irregular masses. Phagocytes next pass into the deeply placed yolk masses, and at the same time the stroma cells of the theca invade the peripheral zones, where the yolk is now absorbed, and the phagocytic cells are disintegrating (Plate VI, fig. 3).

Later stages are characterised by further thecal activity, whereby the outlines of the follicle are obliterated, and the remains of the ovum, represented by scattered yolk masses and phagocytes, are gradually replaced by thecal ingrowth, in the wake of which capillaries develop (Plate VI, fig. 5). The relatively large size sometimes attained by degenerate yolk masses is shown in Plate VI, fig. 4.

In follicles in which the absorption of yolk is apparently more rapid, the phagocytes remain relatively longer before degeneration, and thecal replacement is less prominent, with the result that the theca bounds a group of clear cells surrounding occasional yolk masses (Plate VII, fig. 1). At a stage when the yolk has almost disappeared there remain in the theca multinucleate phagocytes containing granules of brownish yellow pigment; the cytoplasm of other phagocytic cells is vacuolated, probably due to loss of the pigment granules in preparation (Plate VII, fig. 2). These appearances are characteristic

of late stages of yolk absorption. Finally the few remaining phagocytes disintegrate and the follicle is eventually obliterated by the theca. Occasional follicles are observed in which a central cavity, devoid of visible contents, is bounded by phagocytic cells which in some follicles are of the large clear type (Plate VII, fig. 3) and which in others are the later pigmented forms, often multinucleate. These follicles may represent a cystic formation, but it seems more probable that the cavity has contained a single large degenerate yolk mass (the remainder of the ovum undergoing absorption *in situ*) which has been lost in preparation of the sections.

(*c*) *Blood follicles.* The largest ova in these atretic follicles have a diameter of approximately 2·2 mm. in the functional and of 1·5 mm. in the non-functional ovary. In the earliest stages the ovum appears to be quite normal.

The follicle epithelium consists of a single layer of irregularly arranged cubical cells, investing a thin lamina of zona pellucida. The theca interna is distinguished by the oval nuclei of its cells, which are about eight layers deep, and larger than the fibroblasts of the theca externa. The onset of atresia is initiated by a haemorrhage from the thecal capillaries, infiltrating a zone approximately 0·008 mm. thick, beneath the sub-epithelial basement membrane, and bounded externally by a similar membrane consisting evidently of fibres of the theca reticulum, interrupted at intervals by oval theca cells projecting into the haemorrhagic zone (Plate VII, fig. 4). In early stages this blood space, containing red blood corpuscles and occasional leucocytes, does not extend equally about the periphery of the follicle. The haemorrhage progressively separates the epithelium from the theca, the blood space attaining a maximum thickness of 0·05 mm. in some regions (Plate VII, fig. 5). The increased sub-follicular haemorrhage eventually ruptures the follicular epithelium and zona pellucida, the blood cells mingling with the ovular contents and its coverings. The ovular cytoplasm is no longer defined (Plate VIII, figs. 1, 2). The follicular epithelium gives rise to phagocytes of two types—(*a*) cells resembling in appearance those of the normal epithelium, which are associated with the fragmented zona pellucida, as in follicles absorbed *in situ* without haemorrhage, and (*b*) typical phagocytes which ingest yolk globules and later absorb blood pigment. Haemolysis does not occur for some time, the normal form being retained by red blood corpuscles, in the interstices of which fine granules of dark brown pigment are deposited. In follicles in which the blood and yolk remain relatively separate, pigmentation occurs in relation to the area of infiltration, but when the blood and yolk are intimately mingled pigment formation appears to be delayed. Fibrin formation has not been observed. The theca, a thin coat, forms the boundary of the cavity after the separation of the epithelium, and its innermost cells become elongated to form a limiting membrane to the haemorrhage (Plate VIII, fig. 3). The yolk-ingesting phagocytes are first found in the region between the zona pellucida and the theca, and later penetrate centrally amongst the blood corpuscles and yolk, the spheres of which, in the larger follicles, have coalesced to form irregular

degenerate masses. Polymorphs are numerous in some blood follicles at this stage. The yolk is comparatively soon absorbed, but fragments of zona pellucida more deeply situated often remain uninvaded by cells for a longer period. Later the follicular cavity, which becomes reduced, contains a central mass of zona pellucida, fenestrated by phagocytic cells, and pigmented yolk-ingesting phagocytes are present amongst the blood corpuscles (Plate IX, fig. 1).

Pigment formation appears to vary according to the extent of the haemorrhage; in the follicle illustrated in Plate IX, fig. 1 all pigment is intra-cellular, while in some apparently later stages, in which the yolk has been completely absorbed, there is still a large quantity of free pigment as well as that contained in phagocytes (Plate VIII, fig. 4); in other follicles characterised by free pigment granules, clear non-pigmented phagocytes are seen at the periphery of the cavity.

After the disappearance of the zona pellucida and the cells which absorb it, the final stages of resolution set in. A loose network of stellate theca cells advances from the periphery enmeshing the blood corpuscles and pigment-containing phagocytes. At this stage the outer part of the theca is distinguished from this ingrowth by its denser nature (Plate VIII, fig. 4). The reticulum becomes continuously more compact and the blood cells disappear. Finally, the follicular cavity is obliterated by the central coalescence of the thecal ingrowth, and the last stages of blood follicles are represented by fibrous nodules, in the centre of which are small clusters of pigmented cells, as well as extra-cellular pigment (Plate IX, fig. 2).

B. *Rupture atresia*

As in atresia by absorption *in situ*, the ruptured follicles have been divided into two main groups, small follicles in which the absorption of the zona pellucida is the conspicuous feature, and larger follicles in which the outstanding process is the disposal of the yolk content; rupture atresia of the latter is more prevalent. Follicles rupture internally discharging their contents into medullary lacunae, more frequently than externally, in which latter case the ovum and zona pellucida are shed upon the surface of the ovary.

The following types of follicular rupture have been observed:

1. (*a*) Rupture internally of small follicles before yolk formation.

(*b*) Rupture externally of small follicles before yolk formation.

2. (*a*) Rupture internally of large follicles containing heavily yolked ova, with which is sometimes associated haemorrhage from the thecal blood vessels.

(*b*) Rupture externally of large follicles containing heavily yolked ova.

(*c*) Considered separately are some late stages of pigmented follicles ruptured externally, which appear to differ from those of the preceding groups.

1. Small follicles, in both functional and non-functional ovaries, containing ova prior to and during early yolk formation, rupture. Initial stages of this process are lacking in this material.

(*a*) *Small follicles which have ruptured internally.* The cavity of the most recently ruptured follicle measures in its greatest dimensions 0·43 × 0·3 mm. exclusive of the thickened theca, which is differentiated into internal and external layers (Plate IX, fig. 3). The follicle epithelium, composed for the most part of a single layer of cells, becomes folded within the reduced follicular cavity; into these folds there is often an extension of the theca, forming a fibrous core. The zona pellucida, which remains intact and has a thickness of 0·008 mm., conforms to the irregularities thus produced; frequently the ovular contents are washed out in preparation. Protruding through the aperture of rupture, bounded partly by follicle epithelium and partly by theca, the zona pellucida expands in the lacunae into a complex mass, in the folds of which are extruded epithelial cells. The lacunae for the most part are lined by stroma cells, mesothelial in form, which occasionally become mobilised to reinforce the quota of phagocytes derived from the follicle epithelium; the ingestion of the ovular débris in the lacunae is effected by these stroma phagocytes, while those originating in the follicle account in the main for the absorption of the zona pellucida. Ingestion of the material first extruded is always further advanced than that which is in the process of emergence; the smaller folds of the zona pellucida are rapidly disintegrated, leaving isolated masses. During the absorption of these masses, the folds disappear, the zona pellucida becoming homogeneous, and at the same time, with progressive cell invasion, the phagocytes become more numerous peripherally, and often of the pigmented multinucleate form.

Later, during the disappearance of the epithelial lining of the follicle, the vascular theca interna comes to surround the cavity, containing the more compact folded zona pellucida and phagocytic cells, at which stage closure of the point of rupture usually occurs: less frequently, the follicular cavity has been completely separated from the surrounding lacunae while retaining a complete epithelial lining. Fragmentation first occurs in the zona pellucida within the follicle, where later small masses come to be included in the inner region of the theca, which gradually encroaches upon and finally obliterates the follicular cavity (Plate IX, fig. 4).

As a result of absorption of the zona pellucida the follicle is ultimately represented by a fibrous nodule distinguished from the later stages of small follicles absorbed *in situ* by the formation of recent theca in the aperture of the rupture. The zona pellucida persists in the lacunae for some time after obliteration of the follicle, its disintegration being slowly effected by phagocytes in the same way as that of the intra-follicular material; the final stages are represented by a few scattered pigmented phagocytes in the lacunae.

(*b*) *Small follicles which have ruptured externally.* No recently ruptured follicles have been observed, but it appears reasonable to assume that the early changes are similar to those of follicles ruptured internally, there being no remarkable differences, except that the stroma reaction to the discharged follicular contents takes place on the surface of the ovary instead of in the

lacunae. All traces of ovular cytoplasm have been lost. In the most recent follicles the thickened theca forms the boundary of a small cavity, still patent, containing fragmented zona pellucida and follicular epithelial cells. On the surface, at a short distance from the mouth of the follicle, is a flattened folded mass of zona pellucida, in the interstices of which are follicle epithelial cells; surface stroma cells are beginning to invade the extra-follicular zona. In other follicles, at the same phase of degeneration, the aperture has become closed by thecal ingrowth. In a later follicle a distinct layer of epithelial cells remains centrally, although the cavity is obliterated. The inner region of the theca is more active than the thickened fibrous outer portion; a restricted area of which at the point of rupture includes fragments of zona pellucida (Plate IX, fig. 5).

The final stage of this type consists solely of fibrous tissue whose general arrangement indicates the previous follicular changes (Plate X, fig. 1).

2. The rupture of large follicles, containing ova with abundant yolk content, is confined to the functional ovaries.

(*a*) *Large follicles which have ruptured internally.* The most recently ruptured yolk-containing follicles have attained considerable dimensions; in the largest, the maximum diameter of the follicular cavity (including the follicle epithelium) is $2{\cdot}2 \times 0{\cdot}7$ mm. No recently ruptured follicles, intermediate between these and the smaller ones described above, have been observed. The greater part of the ovular cytoplasm and yolk has passed into the adjacent lacunae, whereas the zona pellucida, a sparse and attenuated membrane, and the folded follicle epithelium, are, in the main, retained within the cavity of the follicle and its aperture (Plate X, fig. 2).

Frequently in these stages the capillaries of the theca interna are engorged (Plate X, fig. 2) and small haemorrhages sometimes occur beneath the follicle epithelium, or even into the follicular cavity (Plate X, fig. 3). In parts the epithelial cells, which have increased in size, form a layer several cells deep, with which the zona pellucida is closely associated. An extensive reaction of the stroma cells lining the lacunae occurs around the ovular débris. The wall of the follicular cavity gradually contracts, the follicle epithelium and zona pellucida becoming intimately folded (Plate X, fig. 4). At a stage frequently encountered in follicles of this type, the follicular wall at the point of rupture is still open, and the zona pellucida, invaded by epithelial cells, forms a mass, annular in section, surrounding the remains of the ovum retained within the follicle (Plate XI, fig. 1).

From now on, the cytoplasm is difficult to trace, the yolk does not yet show degenerate changes, although a relatively large quantity remains within the follicular cavity (Plate XI, fig. 1), not infrequently the included ovular material is inconspicuous. A proliferation of the theca lining the aperture ensues, eventually cutting off the follicular cavity. Following the closure of the aperture, resolution is in the main an expression of the activity of the follicle epithelial cells, which invade the zona pellucida, causing its fragmentation, and also give rise to phagocytes which ingest the yolk globules. At this stage

most of the yolk has been absorbed (Plate XI, fig. 2), the small quantity of intra-follicular yolk permitting the acceleration of the process. Later, the fast-diminishing cavity contains only small fragments of zona pellucida and associated cells (Plate XI, fig. 3). All intra-follicular zona pellucida is absorbed, the follicle epithelial cells disappear and at the same time the theca completely obliterates the cavity, resulting in the formation of a fibrous nodule, which cannot be distinguished from the last stages of small ruptured follicles containing ova in which yolk formation has not occurred. A few follicles have ruptured internally at two points in the wall. Judging by the condition of the tissue surrounding the aperture and yolk undergoing absorption in the lacunae, it would appear that the two ruptures occurred simultaneously, or at least at periods not far distant from one another.

Changes in the follicular contents expelled into the lacunae of the medulla of the functional ovary. The medullary region of the functional ovary is composed of vascular fibrous trabeculae, in the interstices of which are lacunae, lined for the most part by flattened cells of the mesothelial type. Following the discharge of zona pellucida ovular cytoplasm, and yolk spheres from a large follicle, the cells of the stroma trabeculae become oval in shape, with deeply staining enlarged nuclei (Plate XII, fig. 3). This cytomorphosis results in large cells, with clear, lightly staining cytoplasm, which proliferate into the yolk-filled spaces, ingesting yolk globules (Plate XII, fig. 4); these stroma phagocytes appear to have the same morphological values as those originating in the follicle epithelium. It would seem that in some instances the stroma reacts rapidly after the rupture of the follicle, in which case the recent yolk is subjected to immediate ingestion; on the other hand, lacunae are observed, evincing no sign of phagocytic proliferation, charged with yolk substance, in a coalesced form in which the outlines of the yolk spherules are frequently apparent (Plate XIII, fig. 2); the significance of this delayed reaction has not been determined.

Yolk absorption proceeds by phagocytic action; yolk in the cytoplasm of the phagocytes is a prevalent feature during early stages (Plate XII, fig. 4–Plate XIII, fig. 3), after which the cytoplasmic inclusions are represented by brownish yellow pigment (Plate XIII, fig. 3). Later, the phagocytic cells by aggregation give rise to multinucleate forms (Plate XIII, figs. 3, 4); after the absorption of the yolk and disappearance of the majority of phagocytes the walls of the lacunae become approximated, although small clusters of pigment-containing cells are seen at intervals (Plate XIII, fig. 6).

The zona pellucida and follicle epithelial cells extruded are in the form of a composite mass (Plate XIII, fig. 1), less extensive than that of small ruptured follicles, confined to the lacunae near the aperture of rupture. Under the influence of the epithelial cells the zona pellucida undergoes early solution (Plate XIII, fig. 4). Not infrequently a reaction takes place in the surface theca cells of the follicle bounding the lacunae, whereby they assume epithelial characters, either cubical or columnar.

In many follicles ruptured internally, which show indications of yolk formation before the onset of atresia, there is a haemorrhage from the thecal vessels; the haemorrhage may be confined to a small area of the follicle, as described above, or may be more severe, filling the follicular cavity, and even extending to the adjacent lacunae. These follicles possess features common to blood follicles absorbed *in situ*, and to large ones ruptured internally. The greater part of the ovular cytoplasm and yolk, together with portions of the zona pellucida and follicle epithelium, are discharged into the lacunae. Ingestion of the material retained in the follicle is accomplished by phagocytes of epithelial origin, while the extra-follicular débris undergoes phagocytosis by the extruded epithelial cells and the cells of the stroma trabeculae. The blood escapes through the still patent aperture of rupture (Plate XII, fig. 1); formation of pigment granules in the interstices of the red blood corpuscles occurs in the intra-follicular blood, but is less constant in that free in the lacunae (Plate XIII, fig. 5); pigment is later absorbed by the yolk-ingesting phagocytes (Plate XIV, fig. 2). In other follicles in which the aperture has become closed, and the disintegration of the ovular material advanced, the blood is confined to the follicular cavity; the thecal vessels of a few follicles in even later stages of resolution are engorged, and the central cavity contains red blood cells, which do not yet appear to be degenerate.

Later changes in these follicles are essentially similar to those in blood follicles absorbed *in situ*, the slight differences being associated with the lesser quantity of ovular material retained in the follicular cavity, and in many instances, with its advanced degeneration before the onset of haemorrhage. The follicle undergoes regression more rapidly than do its contents discharged into the lacunae. Final stages of atretic follicles of this type are represented by fibrous nodules, with a central pigmented region, from which extends a core of similar tissue to the exterior, in the region of rupture (Plate XII, fig. 2).

(*b*) *Large follicles ruptured externally*—after the formation of yolk in the ovum.

No early stages have been observed.

The changes in the material retained in the follicle relate to resolution phases similar to those described in follicles ruptured internally, while the external processes involve the disposal of the follicular débris by stroma cells. Portions of the zona pellucida and some follicular epithelial cells adhere to the surface of the ovary in the vicinity of the rupture; but in no instance is it possible to trace the discharged cytoplasm and yolk. The follicle illustrated in Plate XI, fig. 4 forms the basis of the following description.

A large quantity of yolk has been retained within the follicle, which in sections, not including the point of rupture, closely resembles a large follicle absorbed *in situ* (see Plate VI, figs. 3, 5). Many of the yolk globules have been ingested by phagocytes, while others form irregular degenerate masses, still extra-cellular. Some phagocytes are multinucleate and contain granules of brownish yellow pigment.

Thecal invasion and ingrowth of capillaries is beginning at the periphery. Folds of the zona pellucida, including epithelial cells, extend from the follicle through the aperture, to expand in a flattened mass, for the most part in contact with and invaded by stroma cells. The cells upon the free surface of the follicle form a single columnar layer, distinct from the underlying concentrically arranged fibrous tissue. This reaction of the surface stroma corresponds with the changes seen in lacunae associated with large follicles ruptured internally.

There is one instance of a follicle ruptured externally in which a haemorrhage has occurred at some time. The follicle is represented by a fibrous nodule, containing masses of blood pigment centrally, and at the point of rupture, at a phase a little later than that shown in Plate XII, fig. 2. Upon the external surface is a small amount of zona pellucida invaded by the cells of the stroma.

(*c*) *Late pigmented follicles formerly ruptured externally.* Three functional ovaries contain these bodies, of which there are three in one ovary and two in each of the others. All are similar in general structure, but show variations in development, some being more recent, and others later than that illustrated in Plate XIV, fig. 1.

The follicle is represented by a solid fibrous nodule, merging at the point of rupture with a plug which often projects markedly upon the surface of the ovary (Plate XIV, fig. 1). The inner region of the follicle, which shows a very definite line of demarcation from the external fibrous theca, consists of a vascular fibrous framework containing in its interstices numerous irregularly shaped cells packed with brown pigment, and also occasional enlarged epithelial cells in which no trace of pigment is visible. In most recent stages, the greater part of the plug consists of homogeneous laminae of zona pellucida, sometimes invaded by stroma cells which form a limiting layer superficially. A few degenerate epithelial cells and other pigment-containing cells are included in the folds of zona pellucida. The cells of the free surface of the theca folliculi adjacent to the plug are columnar in form.

In one follicle among the fragmented zona pellucida, and invading fibrous tissue, are several patches of homogeneous material of different staining reaction, closely resembling the large degenerate yolk masses seen in Plate VI, figs. 3–5.

In the latest stages observed, the majority of the pigment-containing cells are vacuolated, and fine extra-cellular pigment granules are scattered in the fibrous tissue, which shows increased vascularity. The plug is reduced in size, appearing only as a slight elevation above the general stroma. The thecal invasion has progressed further, as has also the absorption of the zona pellucida and yolk if present.

DISCUSSION

1. Corpus luteum

It is generally agreed that in the Eutherian Mammals and Marsupials studied, the luteal cells are derived from the follicular epithelium, while thecal ingrowths give rise to the supporting framework of the corpus luteum (Sobotta (mouse)(68), (rabbit)(69), (guinea-pig)(70); Honoré(38) (rabbit); Robinson(63) (ferret); Drips(19) (*Spermophile*); Sandes(65) (*Dasyurus*); O'Donoghue(54,55,56) (Marsupials), and others). Opinions vary with reference to the luteal cells in the lower Vertebrates. Supporters of the epithelial derivation include Giacomini(29) (*Myliobatis*); Wallace(76) (*Zoarces* and *Spinax*); Lucien(48) (*Anguis fragilis* and *Seps chalcides*); Mingazzini(51) (Reptiles); Hett (Birds)(34), (*Colaeus monedula*(35) and *Lacerta agilis*(36)). On the other hand, Cunningham(14) believes that the luteal cells of Teleosts are of thecal origin; and Bühler describes a transitory hypertrophy of the epithelium before its degeneration in Cyclostomes, Teleosts(6) and Amphibia(7); in the Amphibia the cells of the theca later undergo a cytomorphosis. In some Mammals, however, the luteal cells are thought to be derived from thecal as well as epithelial cells. Van der Stricht(75) (Cheiroptera) and Popoff(60) (mole, weasel, dog) state that interstitial cells of the theca take part in the formation of the luteal cells. Corner(12,13) holds the view that in the corpus luteum of the sow, the luteal cells have a dual origin, the majority are epithelial, while the remainder are formed by cells of the theca interna. Gatenby(27), Solomons and Gatenby(71) and Hill and Gatenby(37) have shown that this is not so in the corpus luteum of *Ornithorhynchus*, in which the cells of the theca interna are of a type distinct from the luteal cells, which they believe to be derived from the follicle epithelium. None of the material investigated includes a stage sufficiently recent to shed any light upon this problem; certainly the character of the luteal cells suggests an epithelial rather than a thecal origin.

The early literature of the monotreme corpus luteum by Owen(57) and Caldwell(9) (both of which are reviewed by Hill and Gatenby(37) and by Poulton(61)), based upon insufficient evidence, contributes little to our present knowledge. The results of this investigation conform more closely to the findings of Hill and Gatenby(37), who describe in detail corpora lutea in six different stages of development, and conclude that "the lutein cells arise exclusively from the follicular epithelial cells." In the recently formed corpus luteum, the theca interna cells are represented by "syncytial-like masses and groups, situated partly in their original position between the lutein cells, and the theca externa, partly along the ingrowths of the latter into the luteal tissue." The theca externa gives rise to the fibrous ingrowths, and also to the connective tissue. The earliest stage of this same material was used by Gatenby(27) for comparison with the human corpus luteum, and by Solomons and Gatenby(71).

The following table shows the position of the corpora lutea of this collection (a, b, c, d) in relation to the series of Hill and Gatenby. The classification is based upon the general development of the corpus luteum as well as upon the dimensions of the corpus luteum, luteal cells and intra-uterine ova, the measurements of which are expressed in millimetres.

Stage	Corpus luteum in section (including theca)	Luteal tissue	Luteal cell	Intra-uterine ovum
I. A	2·75 × 2·28	2·6 × 1·97	0·026 × 0·018	6·75
a	2·75 × 2·5 3·04 × 1·6 2·96 × 2·24	2·32 × 2·24 2·9 × 0·88 2·88 × 1·92	0·058 × 0·029	5 and 5·5
II.	4 × 3·12	3·9 × 2·75	0·054 × 0·037	6·5 and 6·75
b	2·88 × 2·32 2·48 × 1·84	2·24 × 1·6 2·32 × 1·04	0·062 × 0·025	4·5 and 5
III.	3·38 × 2·34 3·2 × 2·18	3·2 × 2·18	0·06 × 0·037	6·75 and 7
IV.	3·8 × 2·75	3·7 × 2·6	0·047 × 0·035	9
c	2·88 × 2·83 3 × 2·56	2·56 × 2·24 2·8 × 2·24	—	8
V.	4 × 2·5	3·8 × 2·34	0·047 × 0·03	16·5 × 15
VI.	4·5 × 3·5	—	—	Egg recently laid
d	2·08 × 1·44	1·76 × 0·96	—	No record of egg or young

Hill and Gatenby have stressed the difference in character of the theca of both the follicle and the corpus luteum, in terms of two layers, theca interna and theca externa. Certainly the tissue of the inner region is less fibrous than that farther removed and its cells appear more abundant and more mobilised, although the cell boundaries are not very apparent; transition forms express themselves at all stages, there being no sharp line of demarcation between the two zones. This difference in character of the inner cells appears to be an expression of proliferation, and if there is justification in applying the terms theca interna and externa, they must be understood as terms merely expressing growth activity in one and the same tissue, whether in normal or atretic follicles or in corpora lutea. The findings of this investigation do not support the hypothesis of Hill and Gatenby, who state that "it seems difficult to avoid the conclusion that these theca interna elements subserve in the early corpus luteum a definite secretory function," and that "there is no evidence that they ever take on a fibroblastic activity, even in the regressing corpus luteum."

Since field technique was employed in the fixation of this material, no special staining methods were used for cytological details of the luteal cell. Neither macroscopically nor microscopically is there any evidence of luteal pigment.

It is apparent from Hill and Gatenby's descriptions and from the material investigated that a haemorrhage from the thecal capillaries takes place into

the luteal cavity and through the aperture of rupture to the external surface of the ovary, during or very soon after ovulation. The fibrin clot within the corpus luteum is rapidly invaded by the luteal tissue, whereas that externally is absorbed more slowly by the theca. There is no evidence of an extensive secondary haemorrhage such as has been described in some Mammals.

All corpora lutea observed are of recent formation, apparently associated with one period of the oestrous cycle; it is assumed that the corpora lutea of one sexual season completely disappear before the onset of the next oestrus.

2. Atresia

In the Eutheria, follicular atresia is usually accomplished by absorption *in situ* of the ovum, sometimes accompanied by haemorrhage from the thecal vessels, when it is known as a blood follicle.

Invasion of the zona pellucida and ovum by epithelial cells (Henneguy (33)), and by epithelial and connective tissue cells (Asami (2)), occurs in early follicles before the formation of an antrum folliculi. Asami (2), Henneguy (33), Popoff (60), Van Beneden (73) and Van der Stricht (74) describe a thickening, and in some instances a subsequent folding, of the zona pellucida in follicles at various stages of development. Degeneration of the follicular epithelium (membrana granulosa) is of frequent occurrence in the higher Mammals, according to Allen (1), Asami (2), Delestre (15), De Pinho (16), Hammond and Marshall (31), Heape (32), Henneguy (33), Loeb (45), Marshall (49), Popoff (60), Salazar (64), Van Beneden (73) and Van der Stricht (74). It is the opinion of De Winiwarter (18) that the first indication of atresia is the ingrowth of the theca and its capillaries into the membrana granulosa. There is some doubt as to the origin of the phagocytic cells within the degenerate ovum; supporters of the epithelial derivation include Branca (5), De Pinho (17), Henneguy (33) and Van der Stricht (74). Asami holds the view that the cells are probably epithelial, but that invasion occurs only if the ovum is degenerate. Stockard and Papanicolaou (72) are of the opinion that the chief invading cells are leucocytes, while Newman (53) believes that stroma cells as well as leucocytes fulfil this rôle.

Heape (32) and Hammond and Marshall (31) find that in mature follicles of the rabbit, when ovulation has failed to occur without the necessary stimulus of copulation, blood follicles are formed, the early stages of which are characterised by congestion of the thecal vessels, followed by a haemorrhage into the follicular cavity; phagocytic epithelial cells are seen among the red blood corpuscles, and blood pigment is formed at a later stage. In the Sheep, Marshall (49) observed a few scattered red blood cells in the follicular cavity, but never a blood clot. Parthenogenetic division or degenerative fragmentation of the ovarian ovum, usually accompanied by disintegration of the follicular epithelium, is not infrequent in the Eutheria (Bouin (4), Branca (5), Chappellier (10), Clark (11), Henneguy (33), Janosik (39), Kingery (40), Kingsbury (41), Kirkham (42), Loeb (45, 46), Sansom (66), Stockard and Papanicolaou (72), Van der Stricht (74)). Anovular follicles of two types are described—primitive

anovular follicles, consisting of groups of epithelial cells which have failed to become associated with developing ova (Gérard (28), League and Hartman (43) and Regaud and Lacassagne (62)) and other follicles representing a type of atresia in which the degenerate ovum is replaced by follicular tissue (Gérard (28), League and Hartman (43)).

Follicles may become cystic, in which case, after degeneration of the ovum, the follicular cavity, lined by epithelium, is persistent (Clark (11), Lipschutz and Voss (44)).

The atretic processes in the Marsupial, *Dasyurus viverrinus*, are divided by Sandes (65) into two groups—the atresia of immature follicles, and that of follicles nearing maturity. In the former the degeneration of the membrana granulosa is followed by disintegration of the cells of the discus proligerus and leucocytic invasion; after disappearance of the basal membrane, the theca interna encroaches upon the membrana granulosa. Other immature follicles give rise to a cystic formation, the cavity of which is lined by a single-layered cubical epithelium, into which there is no thecal invasion. In the more mature follicles, the ovum, which may attempt to segment, is invaded by connective tissue and leucocytes, while there is an hypertrophy of the membrana granulosa cells, amongst which there occurs an ingrowth of fibrous tissue, as in typical corpora lutea.

An investigation into the follicular atresia of *Bettongia cuniculus* and other Australian Marsupials is at present in progress.

In the *lower Vertebrates* the ovum may undergo regression by absorption *in situ*, by a formation of blood follicles, or by follicular rupture.

In follicles absorbed *in situ* the majority of writers agree upon the phagocytosis of the ovum by follicle epithelial cells, followed by an ingrowth of the thecal tissue, causing the ultimate obliteration of the follicle. Henneguy (33) finds, in an early follicle in the stork, a marked proliferation of the epithelium, many cells of which include yolk globules. In Birds, Reptiles, Amphibia and Fish, after liquefaction of the ovum, the epithelial cells increase in size and number, and, accompanied by leucocytes, early invade the fragmented ovum. At the same time, blood vessels of the thickened theca penetrate into the follicle epithelium and even into the ovum.

Bühler gives an account of the atresia of Amphibia (7) and Fish (6); after chromatolysis of the egg nucleus, the ovum is invaded by the epithelial cells and leucocytes, and is gradually resorbed; finally a fibrous nodule is formed by the ingrowth of the theca. In recent follicles of the Fish a conspicuous feature is the folded and fragmented oolemma (a structure apparently homologous with the zona pellucida). The most comprehensive account of the atresia of the lower Vertebrates is that of Dubuisson (24), who investigated ovaries of Birds (21,24), Reptiles (22,24), Amphibia (23,24) and Fish (24). In all the follicular epithelium plays the principal part in the absorption of the ovum, in some instances followed by a leucocytic migration; fusion of the yolk spheres is a characteristic feature in Amphibia: in Fish the thickened oolemma is traversed

by phagocytic epithelial cells. It is the opinion of Perez (59)[1] that in some Amphibia, and of Loyez (47)[1], that in Reptiles the follicle epithelium becomes phagocytic in dealing with the degenerate ovum, and obliteration of the follicle is accomplished by growth of the theca. Pearl and Boring (58) describe atretic follicles in the fowl, in which the phagocytes originate entirely in the theca interna, and are similar to groups of epithelioid (interstitial) cells included in the theca.

Although the literature on the ovaries of the lower Vertebrates does not treat of blood follicles as a distinct group, the occurrence of haemorrhagic follicles is evident. In a late atretic follicle of the sparrow, Dubuisson (24) finds red blood corpuscles resulting from a haemorrhage from the dilated thecal vessels during shrinkage of the connective tissue. Red blood cells are also seen in atretic follicles of *Triton*, followed by pigment formation which Dubuisson (20) attributes to blood degeneration; this haemorrhage he believes to be of only secondary importance. Other writers describe pigment in atretic amphibian ova, but as there is no mention of haemorrhage, it would appear reasonable to conclude that in these instances the pigment is intrinsic in the ovum. Pearl and Boring (58) are of the opinion that the pigment of the "luteal cells" (phagocytes derived from the theca interna) of atretic follicles of the fowl is similar to that of the corpus luteum; however, the large pigmented cells amongst the yolk globules in a degenerate follicle closely resemble those of fairly advanced blood follicles, a view supported also by Fell (25). Various stages of blood follicles have been observed in ovaries of certain viviparous lizards now under investigation.

Various stages of ruptured follicles in ovaries of the fowl and the sparrow have been encountered by Dubuisson (21, 24), whose descriptions suggest a similar process also in the pigeon and in the fish (*Salmo umbla*). The most recent appear to be those of the fowl (24), which he likens to "collapsed balloons" (Stage III), where the thin thecal wall has ruptured, and the follicular contents have been expelled into neighbouring lacunae; the follicular cavity contains remnants of cytoplasm and phagocytes of epithelial origin, some of which have migrated through the orifice to the lacunae. It is noteworthy that these follicles have not attained mature dimensions, and Dubuisson concludes that normal ovulation could not have taken place. At a later stage (Stage II) the theca is of considerable thickness, but at one point is thin—in Dubuisson's opinion, a presage of rupture; it appears more probable that rupture has occurred and the aperture closed. Further degeneration is indicated in descriptions of follicles of the sparrow; a point Dubuisson considers of interest is that whereas the tissue of the thickened theca is usually concentrically arranged, at one spot a wedged plug is formed, with the apex directed externally; the phagocytic epithelial cells within the follicle are about eight rows deep and penetrate between the limbs of the V as if extruded from the interior; these

[1] Perez, Loyez. These papers were not accessible; the views of Perez are stated by Marshall (50), and the work of Loyez is reviewed by Dubuisson (24).

cells are of a syncytial nature, but become detached as spherical elements in the lacunae. Dubuisson notes the similarity of the intra-follicular phagocytes to those in the lacunae, and is in doubt as to whether the epithelial cells have traversed the theca, or whether the cells in the lacunae originate in the stroma wall to which they appear attached at some points; he is of the opinion that the phagocytes pass from the lacunae into the blood vessels. Near one follicle of the pigeon, in which there is an indication of rupture of the thecal wall, the lacunae contain vacuolated phagocytes which have ingested yolk spheres. An observation of interest is that in the sparrow rupture may occur at several points in the follicular wall. It is possible to place a similar interpretation upon Dubuisson's description of some atretic follicles of *S. umbla* (24), in which the epithelial phagocytes penetrate the theca and finally migrate to blood vessels or adjacent lacunae; the penetration of these elements is irregular and at some points causes considerable dissociation of the theca. Occasional ruptured follicles are seen in ovaries of some viviparous lizards, in which the atretic processes appear in the main similar to those of *Ornithorhynchus*; these observations are due for immediate publication.

Follicular atresia in *Ornithorhynchus* is mentioned briefly by Hill and Gatenby (37), who state that "in the small atretic follicles the degenerate contents are apparently resorbed *in situ*, but in the larger they would usually appear to be discharged directly through a break in the follicular wall into an underlying lymph sinus." They give a more detailed account of two follicles of the latter type which they believe to be peculiar to *Ornithorhynchus*.

It will be seen that the atretic processes of *Ornithorhynchus* have some features in common with those of the Eutheria and Metatheria, whose ova are devoid of any appreciable yolk-content, but resemble more closely those of the lower Vertebrates, with heavily yolked ova. The essential differences in the atresia of the Monotremes and lower Vertebrates from those of the higher Mammals are associated with:

1. The large dimensions of the ovum and its yolk-content.
2. The bulk of the zona pellucida surrounding the large ovum.
3. The single-layered condition of the follicle epithelium.
4. The absence of follicular cavity and liquor folliculi.

In all types of atresia in *Ornithorhynchus* the cells of the follicle epithelium have a phagocytic rôle in the absorption of the ovum and the investing zona pellucida. Of the follicles absorbed *in situ* the outstanding feature of the smaller is the folding of the thickened zona pellucida, and its subsequent fragmentation. The larger follicles are characterised by the comparatively rapid disappearance of this membrane, and the absorption of the large yolk-content by phagocytic cells, amongst which the thecal ingrowth begins before the final disappearance of the yolk masses. The activity of the follicle epithelium and the increase in bulk of the zona pellucida, together with the degeneration of the ovum, in the smaller follicles, suggests that the follicle epithelium takes part in the formation of the zona pellucida.

Although leucocytic invasion is prevalent in atretic follicles of other Vertebrates, leucocytes are encountered only in blood follicles of *Ornithorhynchus*, where they appear to be associated with the haemorrhage, rather than with an active migration. In the small follicles affected by rupture atresia the zona pellucida is most conspicuous, while in the larger follicles it is absorbed long before the disappearance of the yolk. In the small ruptured follicles (Plate IX, fig. 3) the appearance of the intra-follicular epithelium closely resembles that of small follicles absorbed *in situ* (Plate XIV, fig. 3), but is more probably associated with contraction and folding of the wall than with active ingrowth, as in the latter type. No recently ruptured follicles have been observed intermediate in size between the large (2 × 2·7 mm.) and the smaller yolkless forms; however, later stages of follicles containing yolk-laden ova would seem to indicate that rupture may occur at intermediate stages.

It is evident that haemorrhage from the thecal vessels may occur during, or at any period subsequent to, the rupture of the follicular wall; slight haemorrhage is seen in some large recently ruptured follicles (Plate X, fig. 3), but in many follicles, in which the haemorrhage fills the follicular cavity and extends to the lacunae, the ovular material has undergone degenerative change, while the thecal vessels appear engorged and the blood retains a normal appearance. It is assumed that the haemorrhage has taken place after the closure of the aperture of rupture in follicles in which the blood is confined to the follicular cavity, and which otherwise show advanced regression. It is impossible to say whether follicles, normal except for a sub-epithelial haemorrhage (Plate VII, figs. 4, 5), represent early stages of follicles destined to rupture, as well as of blood follicles absorbed *in situ*.

An exceptional feature is seen in three recently ruptured blood follicles of one *Echidna* ovary; a haemorrhagic zone separates the follicle epithelium from the theca, and extends to the follicular cavity, and through the patent aperture to the lacunae, which also contain ovular débris and phagocytic cells. The epithelium within the follicle forms a folded layer in parts about ten cells deep; probably this proliferation is an exaggeration of the usual multiplication to form phagocytes; it is reminiscent of "atretic corpora lutea," described in some Mammals, in which there is an attempt at luteal cell formation in atretic follicles. In ruptured follicles of the *Platypus* the epithelium retained in the follicle destroys the remaining ovular débris, while that expelled with the greater part of the zona pellucida assists in the absorption of the latter; other phagocytes originate in the stroma trabeculae, and ingest the displaced yolk spheres. The yolk-ingesting cells of follicles absorbed *in situ*, and in the lacunae associated with ruptured follicles, later contain a brownish yellow pigment; Dubuisson (24) describes a similar pigment in epithelial cells included in theca of atretic follicles of the Fish, and Popoff (60) finds that epithelial cells in the centre of the atretic follicle, as well as interstitial cells throughout the cortical region of the ovary, contain a yellowish pigment, and states that this condition is also observed by Mulon (52) in the guinea-pig.

Hill and Gatenby (37) are of the opinion that in the *Platypus* the lacunae of the medulla of the functional ovary are of the nature of lymph sinuses, into which are discharged the contents of the atretic follicle. Certainly, they represent potential spaces in the stroma, whose temporary distension is caused by the expulsion of the follicular contents.

The medullary region of the non-functional ovary is composed of more compact stroma, with few and small lacunae, and nowhere has the reticular appearance characteristic of that of functional ovaries; this formation would appear to be associated with the fact that here the follicles never attain great dimensions and, therefore, the quantity of material expelled from the ruptured follicles would be smaller in amount.

Follicular atresia does not appear to be directly dependent upon the presence of corpora lutea (as Sandes (65) believes in the Marsupial, *Dasyurus viverrinus*), since atretic follicles occur with equal frequency in ovaries in which ovulation has not recently taken place. All ovaries investigated contain follicles in the process of absorption *in situ*; ruptured follicles are most prevalent in two ovaries (*P. VII* and *P. VI*) with corpora lutea; in the former these follicles are mostly small, prior to yolk formation, while in the latter they are of large size and extremely numerous. Two ovaries (*P. III* and *P. IV*), taken during the breeding season, contain many ruptured follicles in which the haemorrhage has been severe, as well as several blood follicles absorbed *in situ*, but corpora lutea are absent.

With the data available, and the absence of evidence relating to ovulation and copulation, it is not possible to come to any conclusions regarding the cyclic degeneration of follicles, or to associate the different types of atresia with the physiological changes of the oestrous cycle.

SUMMARY

1. In the corpus luteum of *Ornithorhynchus*, the luteal cells appear to be derived from cells of the follicle epithelium.

2. Atresia may overtake ovarian follicles containing ova 0·3–0·4 mm. in diameter, and at all subsequent stages of development.

3. All ovarian follicles in non-functional ovaries become atretic before reaching maturity, the dimensions of the largest normal ovum observed being 1·3 mm.

4. Atretic follicles may be divided into two types:

A. Those absorbed *in situ*.

B. Those which rupture (1) internally or (2) externally.

5. In Group A the follicle epithelium by proliferation and migration gives rise to phagocytes which dispose of the follicular contents.

6. In Group B the ovular débris expelled into the medullary lacunae is mainly ingested by stroma phagocytes of the same morphological value as those of epithelial origin in follicles absorbed *in situ*, the former are assisted

by epithelial phagocytes for the most part associated with the discharged zona pellucida. Epithelial phagocytes dispose of the remaining intra-follicular material.

7. In group B 2 the greater part of the ovular débris shed upon the surface of the ovary is lost in the peritoneal cavity, or gains the oviduct in cases where the ovary is enveloped by the Fallopian tube: the small amount of ovular material remaining adherent to the ovary is invaded by displaced follicular epithelial cells, and cells of the cortical stroma.

8. Haemorrhage from the thecal capillaries may occur in follicles of both types A and B.

9. Atresia in *Ornithorhynchus* is comparable to that in Sauropsida, Amphibia and Pisces, all of which possess ovarian follicles devoid of an antrum folliculi, and containing heavily yolk-laden ova.

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EXPLANATION OF PLATES

Plate I

Fig. 1. Group of small histologically normal follicles; the smallest ova have a diameter of 0·08 mm. the follicle epithelium is subcubical or cubical and zona pellucida is lacking. (×117.)

Fig. 2. Normal follicle, containing ovum of 0·4 mm. diameter, showing first indications of yolk formation. The zona pellucida lies internal to the cubical follicle epithelium. (×117.)

Fig. 3. Normal follicle, containing ovum of 0·66 mm. diameter at a stage later than the maximum thickness attained by the zona pellucida, exhibiting more advanced yolk formation in a zone between peripheral and central yolk-free regions. Differentiation of the theca is beginning. (×117.)

Fig. 4. Portion of wall of normal follicle, containing ovum nearing maturity, of 2·5 mm. diameter. The follicle epithelium surrounds the attenuated zona pellucida. Thecal interna and externa can be distinguished. (×117).

Plate II

Fig. 1. Corpus luteum, Stage *a*. The Fallopian tube is applied to the free surface of the ovary. Large blood vessels are seen in the fibrous theca externa; extending into the luteal tissue are thecal ingrowths, at the apices of which groups of theca interna cells are most conspicuous. The central fibrin cavity is not yet obliterated. (×34.)

Fig. 2. Corpus luteum, Stage *b*. The central cavity is almost obliterated, and groups of theca interna cells are less conspicuous at the periphery of the luteal tissue. (×34.)

Fig. 3. Corpus luteum, Stage *c*, characterised by a thin theca externa, and greater bulk of luteal tissue, in which the majority of luteal cells exhibit degenerative changes. A fibrin mass is seen on the surface at *X*. (×34.)

Fig. 4. Corpus luteum, Stage *d*, composed mainly of fibrous tissue. Theca interna cells are most marked at the junction of the theca externa and the former luteal tissue. A fibrin mass is included in the theca in the region of rupture at *X*. (×34.)

Plate III

Fig. 1. Portion of wall of corpus luteum, Stage *a*, showing the thecal ingrowths into the luteal tissue; theca interna cells are most prevalent at the apices of the processes, and penetrate between individual luteal cells. The central cavity contains fibrin and leucocytes. (×117.)

Fig. 2. Portion of wall of corpus luteum, Stage *b*. Capillaries enter the periphery of luteal tissue from the theca externa. Groups of theca interna cells are less conspicuous, while the cellular network between the luteal cells is further developed. Some luteal cells contain cytoplasmic vacuoles. Fibrin and leucocytes are seen in the reduced central cavity at *X*. (×148.)

Fig. 3. Portion of central region of luteal tissue of corpus luteum, Stage *c*, showing complex capillary system and network of theca cells between luteal cells. The majority of luteal cells evince degenerative changes; a cytoplasmic vacuole containing a granular sphere appears in the centre of the field; pyknotic and vacuolated nuclei are prevalent. (×148.)

Fig. 4. Portion of central fibrous core of corpus luteum, Stage *c*. Luteal cells are characterised by pyknotic and vacuolated nuclei, and cytoplasmic vacuoles; leucocytic invasion is marked. (×148.)

Plate IV

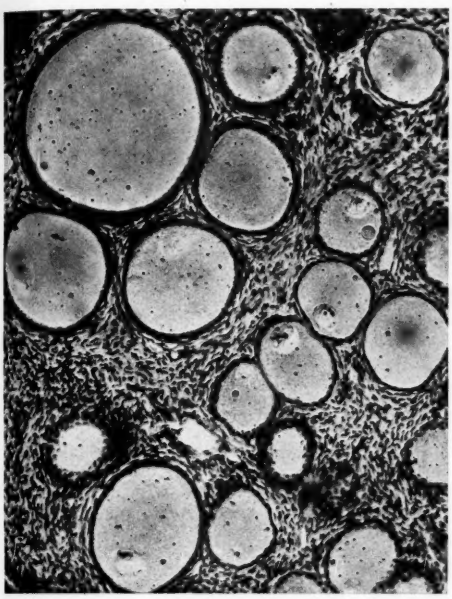
Fig. 1. Portion of wall of corpus luteum, Stage *d*. Within the theca externa, groups of darkly staining theca interna cells occur at the periphery of the luteal tissue. (×148.)

Fig. 2. Portion of the central region of luteal tissue of corpus luteum, Stage *d*. Amongst the fibrous tissue are occasional degenerate luteal cells, represented by pyknotic or vacuolated nuclei, and others with cytoplasmic vacuoles containing granular spheres. (×148.)

Figs. 3 and 4, Plate IV, and figs. 1–4, Plate V, illustrate atresia of small follicles by absorption *in situ*.

Fig. 3. Atretic follicle characterised by proliferation and ingrowth of follicle epithelium beneath the thickened zona pellucida into the degenerate ovum. (×148.)

Fig. 4. Atretic follicle, showing invasion of zona pellucida by follicle, epithelial cells also seen entering the degenerate ovular cytoplasm. (×148.)



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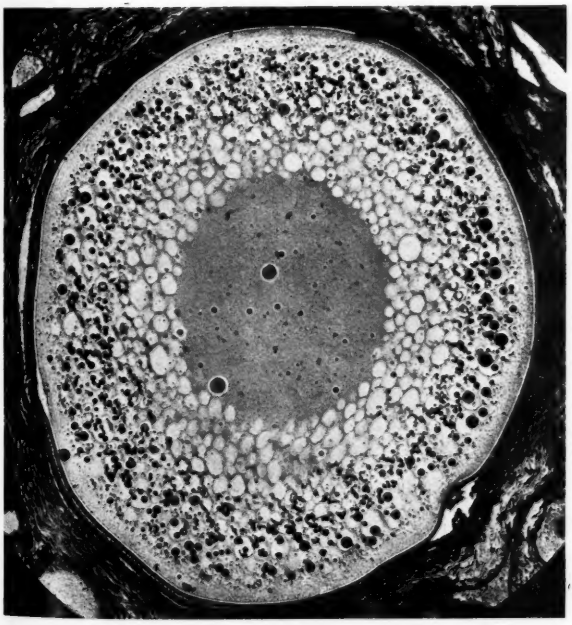

Fig. 3

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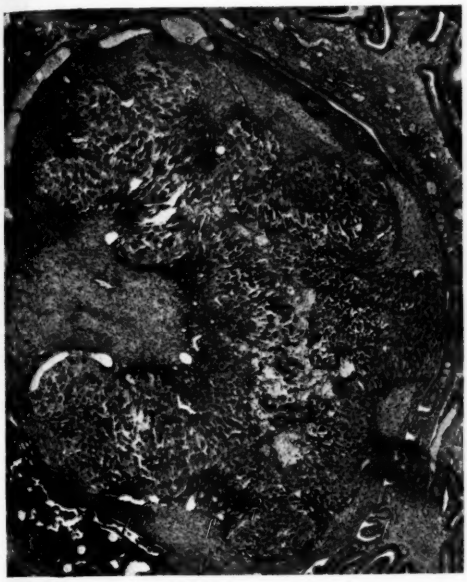

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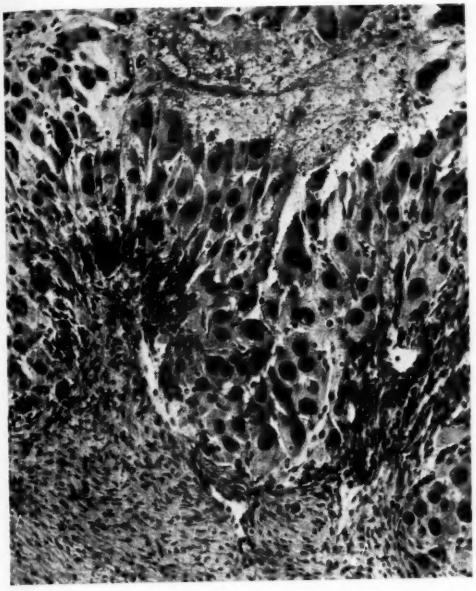

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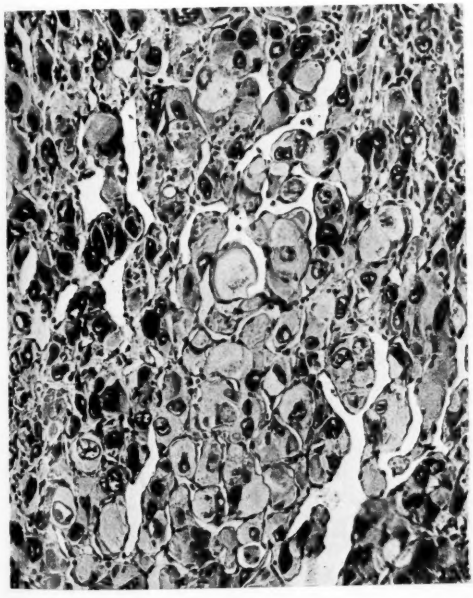

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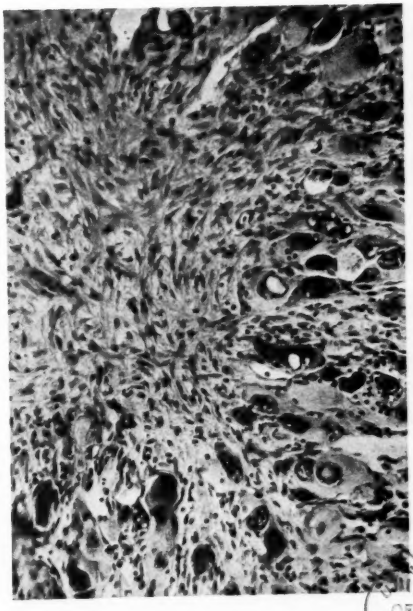

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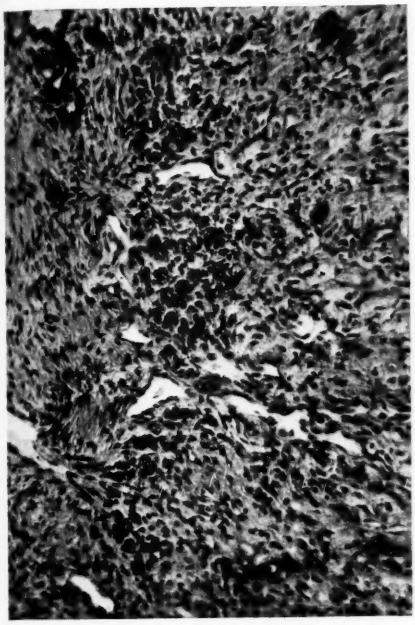

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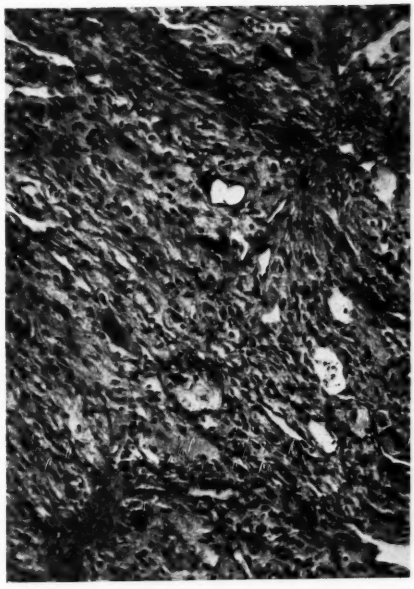

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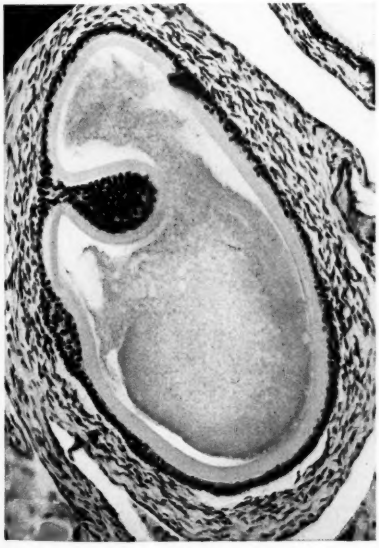

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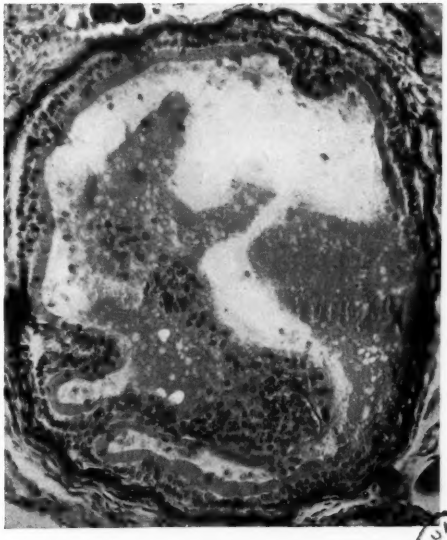

Fig. 4

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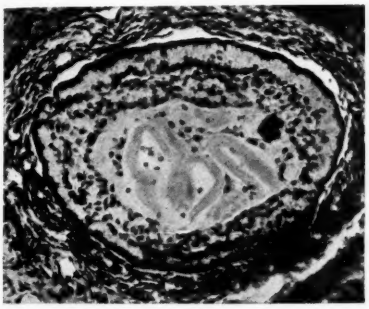

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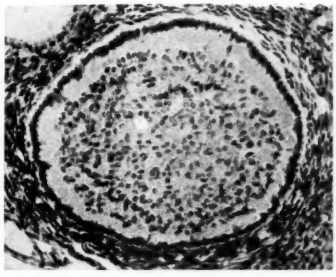

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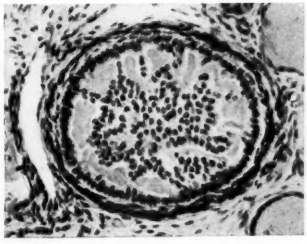

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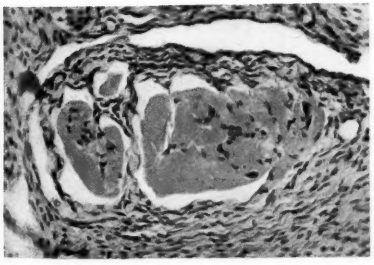

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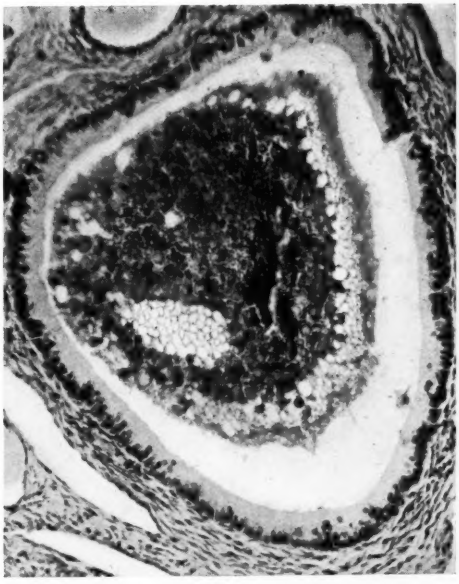

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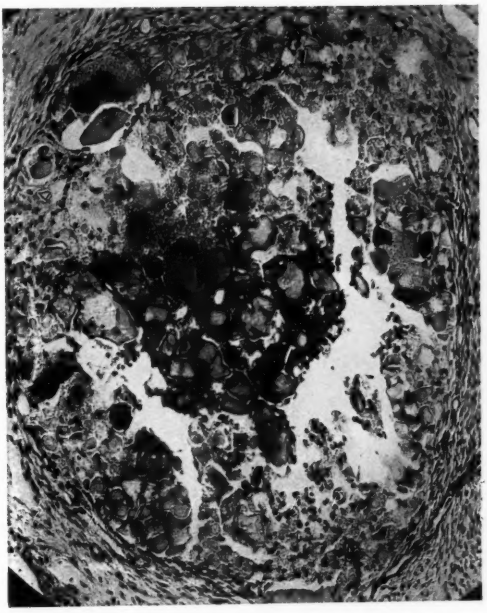

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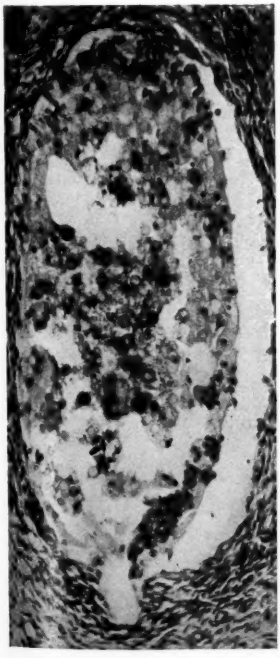

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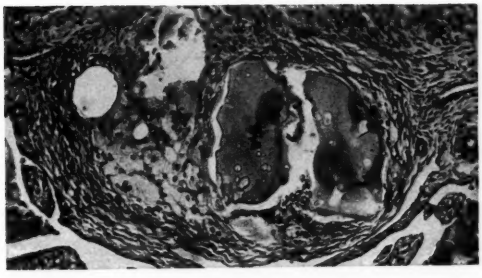

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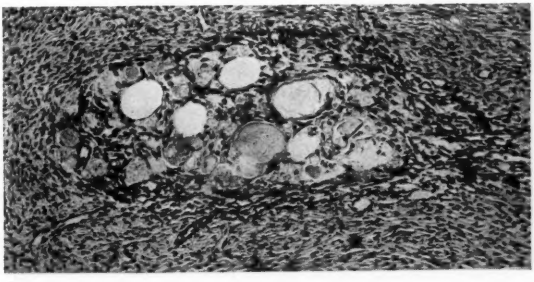

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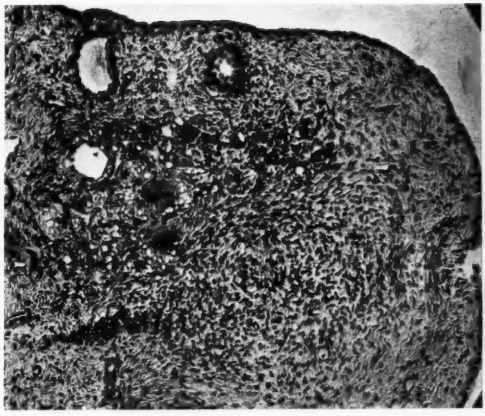

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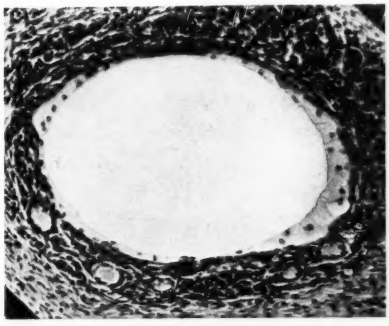

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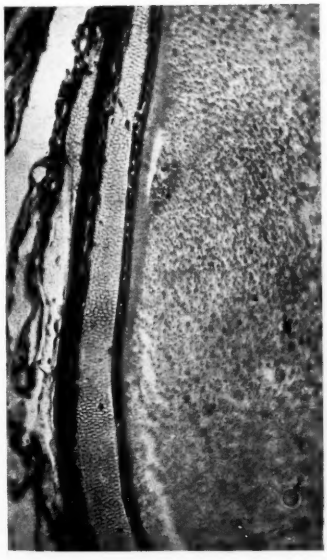

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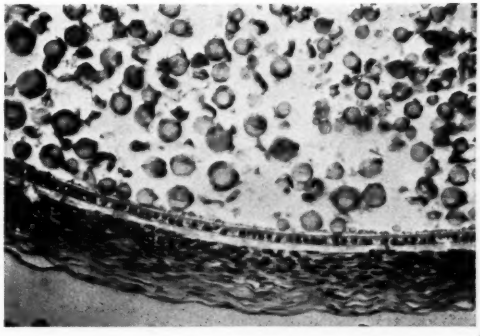

Fig. 4

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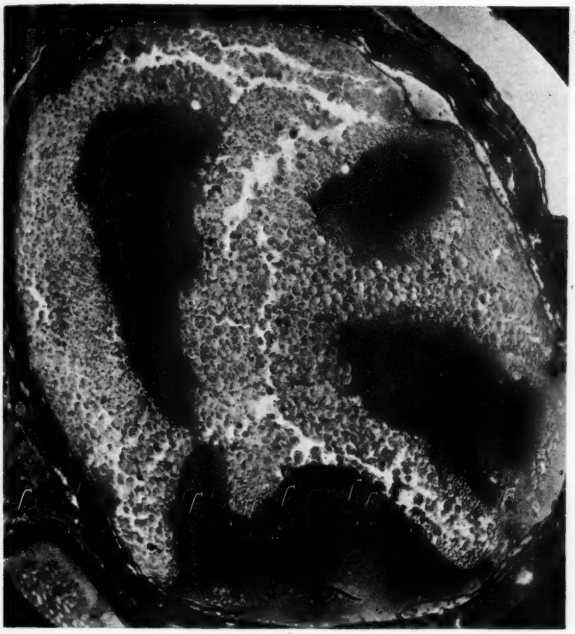

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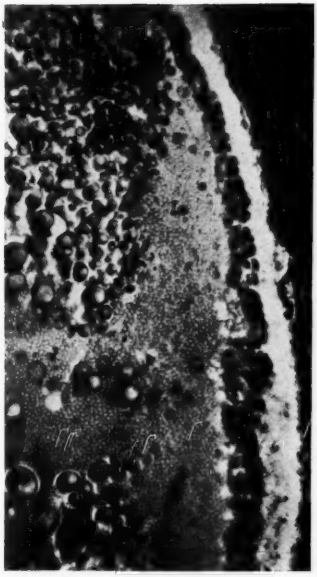


Fig. 2

Fig. 4

Fig. 3

PLATE V

Fig. 1. Atretic follicle, showing further invasion of ovum by follicle epithelial cells. Folds of zona pellucida and phagocytic epithelial cells occupy the central region. (× 148.)

Fig. 2. Atretic follicle in which epithelial cells have penetrated throughout the ovum, leaving the fragmented zona pellucida as an irregular peripheral layer. (× 148.)

Fig. 3. Atretic follicle in which the zona pellucida appears as a sinuous fragmented layer peripherally. (× 148.)

Fig. 4. Late stage of atretic follicle, after disappearance of follicle epithelium as a bounding layer. Fragments of zona pellucida sewn with phagocytic epithelial cells are surrounded directly by the theca. (× 148.)

Figs. 5 and 6 (Plate V), figs. 1–5 (Plate VI), and figs. 1–3 (Plate VII) illustrate atresia of larger follicles by absorption *in situ*.

Fig. 5. Atretic follicle, showing increase in follicle epithelium thickening of zona pellucida, and degenerative changes in ovular substance. (× 148.)

Fig. 6. Atretic follicle, showing invasion by epithelial cells and fragmentation of zona pellucida, and degenerate appearance of ovular cytoplasm and yolk. (× 148.)

PLATE VI

Fig. 1. Atretic follicle in which the zona pellucida is thickly sewn with epithelial cells, others of which have penetrated to the degenerate ovular material, and have assumed the phagocytic form. The follicle epithelium and zona pellucida have been separated artificially from the theca. (× 108.)

Fig. 2. Atretic follicle, showing further invasion of ovum by epithelial phagocytes, many of which at the periphery of the follicle are in the form of degenerate multinucleate masses. (× 148.)

Fig. 3. Atretic follicle in which yolk globules have coalesced before penetration of phagocytes to the central region. Thecal ingrowth is beginning peripherally between the phagocytic cells and small yolk masses. (× 108.)

Fig. 4. Atretic follicle, illustrating large size attained by degenerate yolk masses, which contain multinucleate degenerate phagocytes. (× 108.)

Fig. 5. Atretic follicle in which absorption of yolk and thecal ingrowth is further advanced. In this and the preceding figure (fig. 4) some yolk masses have washed out in preparation. (× 117.)

PLATE VII

Fig. 1. Atretic follicle in which phagocytic cells remain after absorption of the greater part of the yolk; thecal ingrowth occurs between the peripheral degenerating phagocytes. (× 117.)

Fig. 2. Late stage of atretic follicle, showing multinucleate pigment-containing phagocytes in the fibrous thecal tissue, which has obliterated the follicle. (× 117.)

Fig. 3. Atretic follicle of "cystic" appearance; fragments of zona pellucida are included in the active internal region of the theca; the cavity is lined by cells of phagocytic type. (× 148.)

Figs. 4 and 5 (Plate VII), figs. 1–4 (Plate VIII), and figs. 1 and 2 (Plate IX) illustrate blood follicles absorbed *in situ*.

Fig. 4. Portion of follicular wall, showing first indications of formation of blood follicle. The follicle epithelium is separated from the theca by a narrow haemorrhagic zone, whose internal boundary is formed by the basement membrane of the epithelium. (× 148.)

Fig. 5. Portion of the follicular wall, showing increase in haemorrhagic zone between follicle epithelium and theca. (× 148.)

PLATE VIII

Fig. 1. Atretic follicle, showing rupture of follicle epithelium and zona pellucida by haemorrhage into ovum. (× 64.)

Fig. 2. Portion of wall of atretic follicle, showing haemorrhagic zone between the intimately folded follicle epithelium and zona pellucida, and the theca; blood corpuscles are seen amongst the yolk globules of the ovum. (× 148.)

Fig. 3. Atretic follicle after absorption of yolk, showing follicular cavity, bounded by theca, and containing red blood corpuscles, in the interstices of which pigment formation has occurred. In the cavity are seen also a folded mass of zona pellucida and epithelial cells, and a few scattered pigmented phagocytes. (× 64.)

Fig. 4. Atretic follicle, showing ingrowth of theca reticulum (in which are enmeshed pigment-containing phagocytes) into the follicular cavity filled with blood corpuscles, amongst which pigment has been formed. (× 87.)

Plate IX

Fig. 1. Atretic follicle, showing blood cavity containing a folded mass of zona pellucida and epithelial cells, and phagocytes which have ingested yolk spheres and blood pigment. (× 108.)

Fig. 2. Late stage of blood follicle, the cavity of which has been obliterated by thecal growth, in the central region of which are large pigment-containing phagocytes. (× 108.)

Figs. 3–5 (Plate IX), and fig. 1 (Plate X) illustrate rupture atresia of small follicles.

Fig. 3. Small follicle ruptured internally. The follicle epithelium and thickened zona pellucida retained in the follicle are thrown into folds, while the greater part protrudes through the aperture of rupture to adjacent lacunae. Epithelial cells are extruded with folds of zona pellucida. (× 117.)

Fig. 4. Small follicle ruptured internally. The follicular cavity has been obliterated by thecal ingrowth. Masses of zona pellucida are included in the inner region of the theca; in adjacent lacunae are seen phagocytic cells. (× 117.)

Fig. 5. Small follicle ruptured internally. Although the follicular cavity has been obliterated, some epithelial cells remain in the central region. Fragments of zona pellucida are included in the theca at the site of rupture, at *X*. (× 117.)

Plate X

Fig. 1. Resolution stage of small follicle ruptured externally, showing arrangement of fibrous tissue of central region and tissue at point of rupture. (× 117.)

Figs. 2–4 (Plate X), figs. 1–4 (Plate XI), and figs. 1–2 (Plate XII) illustrate rupture atresia of large follicles.

Fig. 2. Large follicle ruptured internally. The follicular cavity contains folded follicle epithelium and adherent zona pellucida, together with a small quantity of yolk and cytoplasm. The capillaries of the inner region of the theca are engorged. Yolk spheres are seen in lacunae adjacent to the follicle. (× 62.)

Fig. 3. Portion of wall of large follicle ruptured internally, showing thecal capillaries, and haemorrhagic zone amidst follicle epithelial cells beneath thin zona pellucida. The field shows a fold of epithelium and zona pellucida protruding into the follicular cavity. (× 148.)

Fig. 4. Large follicle ruptured internally, showing engorged vessels of theca interna, and folding of follicle epithelium and zona pellucida. The ovular material has been discharged from the follicle; the plane of section does not include the point of rupture. (× 62.)

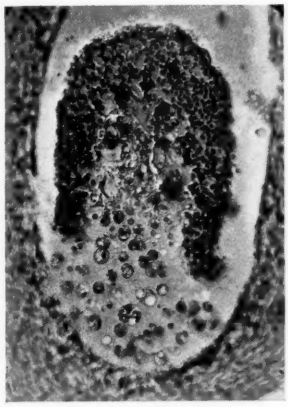
Plate XI

Fig. 1. Large follicle ruptured internally. The follicular cavity contains yolk globules and a folded mass of zona pellucida and epithelial cells; the latter have been separated artificially from the theca. The aperture of rupture is not shown in this section. (× 117.)

Fig. 2. Large follicle ruptured internally, showing fragments of zona pellucida and phagocytic epithelial cells in follicular cavity; the aperture of rupture (as *X*) has become closed. (× 117.)

Fig. 3. Large follicle ruptured internally. The cavity contains fragments of zona pellucida and epithelial cells. Included in the thecal tissue in the region of rupture is a small mass of zona pellucida. (× 117.)

Fig. 4. Large follicle ruptured externally; a folded mass of zona pellucida, with associated epithelial cells, protrudes through the aperture of rupture to the external surface. The follicular cavity is occupied by degenerate yolk and phagocytes, at the periphery of which thecal ingrowth occurs. (× 117.)



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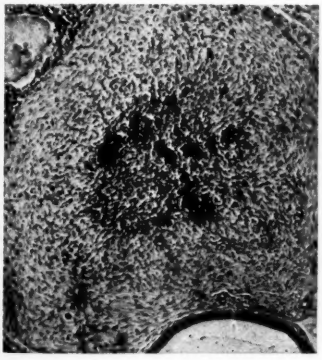

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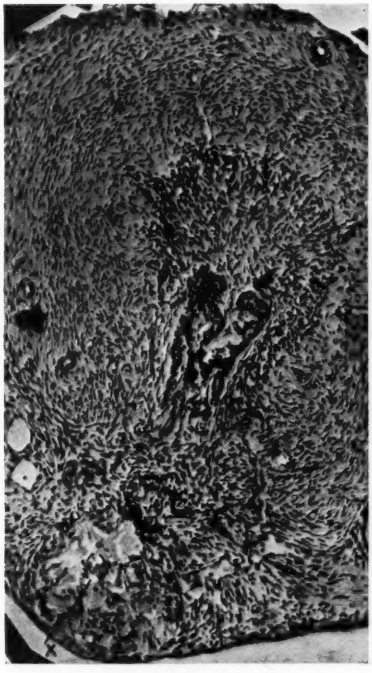

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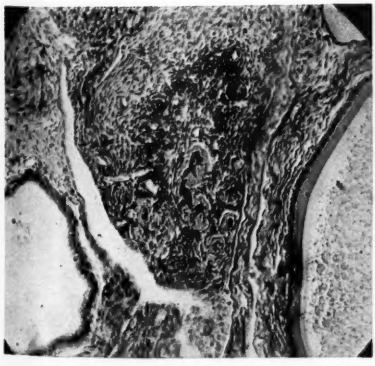

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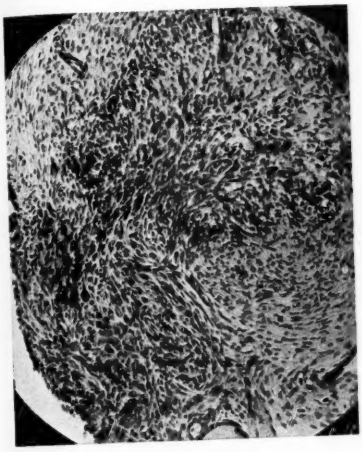

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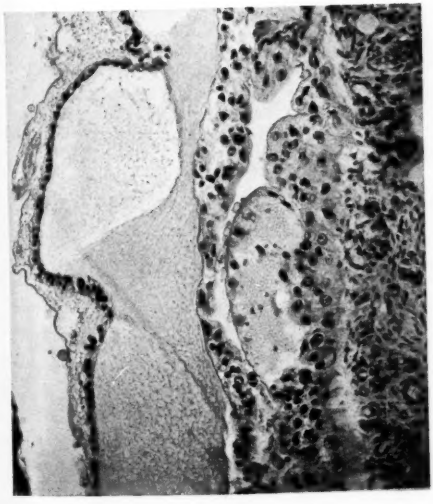

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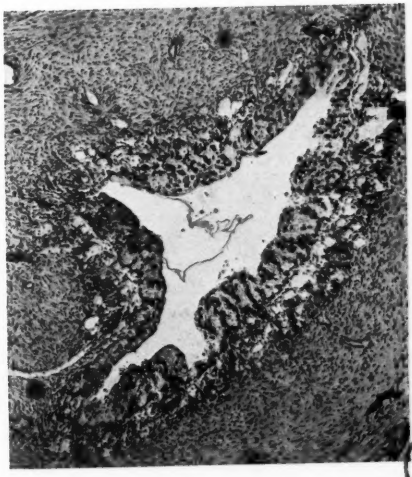

Fig. 4

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Fig. 1

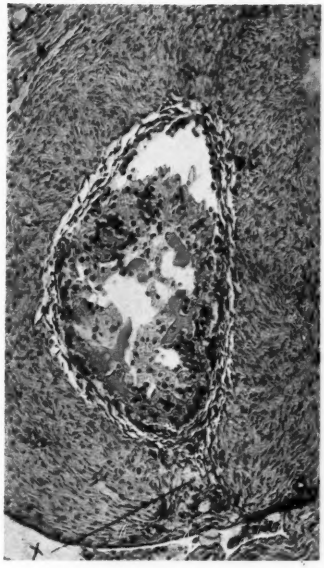
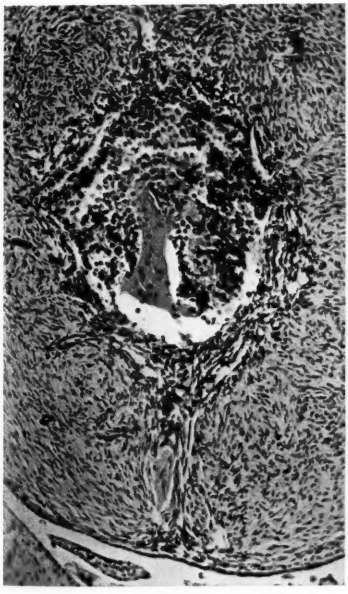


Fig. 2



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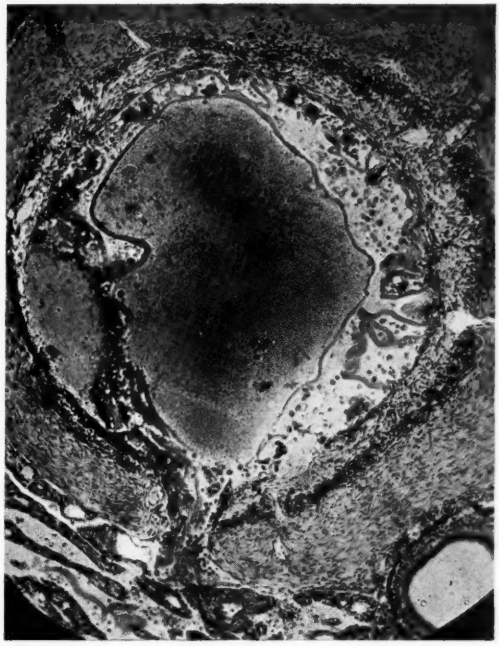

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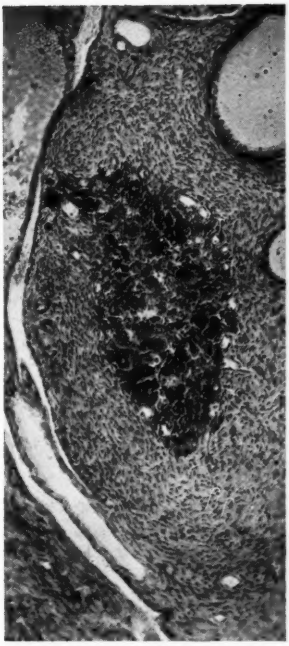

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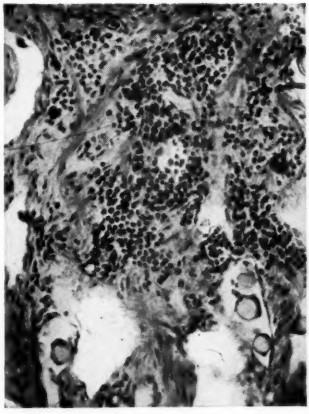

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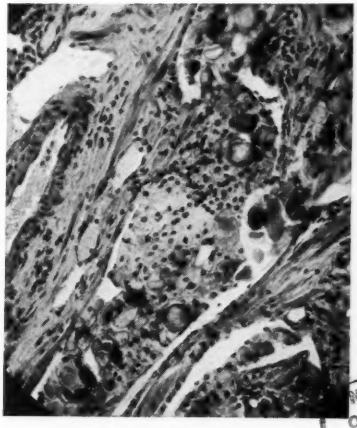

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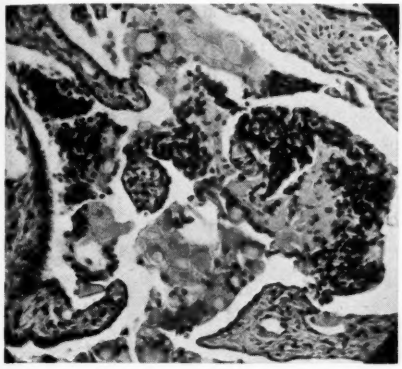

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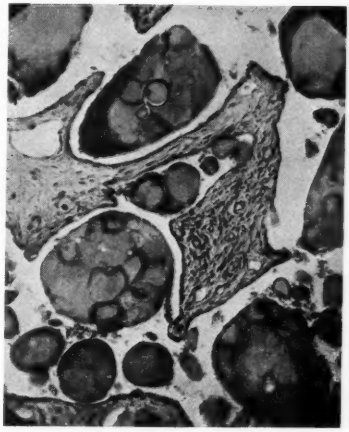

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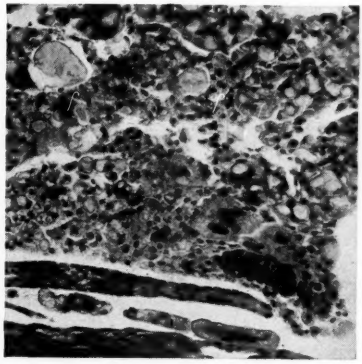

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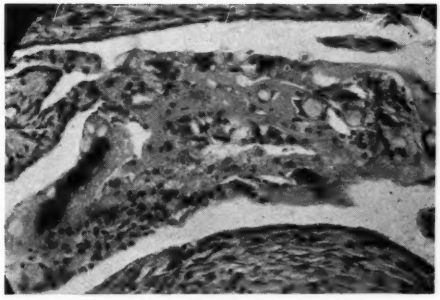

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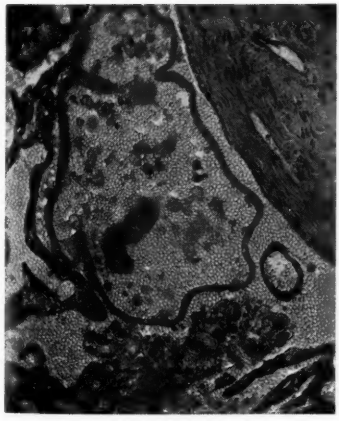

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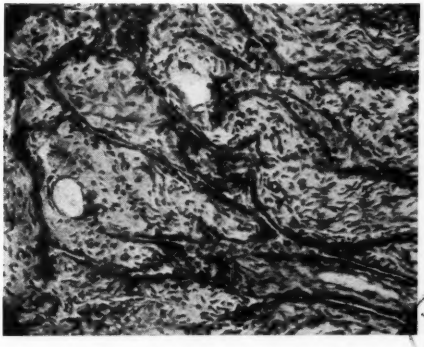

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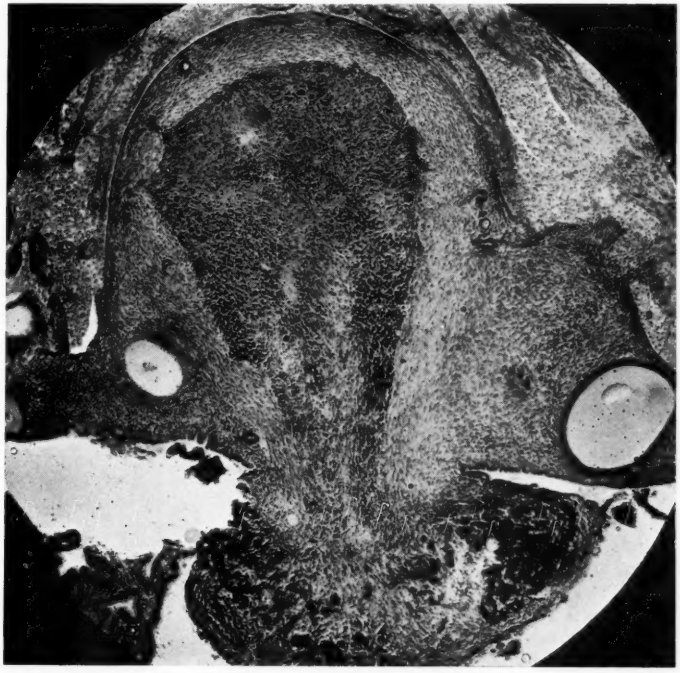

Fig. 1

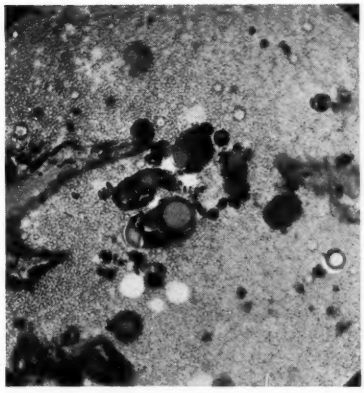

Fig. 2

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PLATE XII

Fig. 1. Large follicle ruptured internally. Haemorrhage from engorged thecal capillaries fills the follicular cavity and extends through the aperture of rupture to adjacent lacunae. The zona pellucida in the follicle and in the lacunae is thrown into folds. Phagocytic epithelial cells are most prevalent in the peripheral region of the follicular cavity; blood pigment has been formed centrally. (× 87.)

Fig. 2. Late stage of haemorrhagic ruptured follicle, showing thecal nodule with pigment-containing phagocytes centrally, and extending throughout the region of rupture. (× 117.)

Figs. 3 and 4 (Plate XII), figs. 1–6 (Plate XIII), and fig. 2 (Plate XIV) illustrate medullary lacunae of functional ovaries associated with large follicles ruptured internally.

Fig. 3. Portion of medullary region, showing first stages of stroma reaction to ovular débris newly discharged from ruptured follicle. (× 148.)

Fig. 4. Lacunae, containing yolk globules and phagocytic cells, the latter in parts being continuous with the tissue of the stroma trabeculae. (× 148.)

PLATE XIII

Fig. 1. Lacunae adjacent to aperture of ruptured follicle (shown in fig. 1, Plate XI). In the lacunae are seen folded masses of zona pellucida, and darkly staining epithelial cells, as well as yolk globules undergoing ingestion by stroma phagocytes. (× 148.)

Fig. 2. Lacunae in which yolk globules have coalesced to form large masses, in some of which outlines of original spheres can be seen. Cellular reaction appears to be delayed. (× 148.)

Fig. 3. Later stage of yolk ingestion in lacunae, by stroma phagocytes, some of which are of degenerate multinucleate form. (× 148.)

Fig. 4. Lacunae, containing yolk-ingesting phagocytes and homogeneous zona pellucida, the folds of which include epithelial cells. A large multinucleate phagocyte is seen at the left of the field. (× 148.)

Fig. 5. Lacunae, containing haemorrhage from ruptured follicle (shown in fig. 1, Plate XII) and also fragments of zona pellucida, degenerate yolk, and phagocytic cells. (× 148.)

Fig. 6. Medullary region, showing apposition of stroma walls of lacunae after absorption of ovular débris from ruptured follicle. The lacunae contain occasional degenerate phagocytic cells. (× 148.)

PLATE XIV

Fig. 1. Late stage of large follicle ruptured externally, consisting mainly of fibrous tissue, in the inner region of which are numerous pigmented cells and occasional larger cells of epithelioid appearance. The projecting plug region is composed of fibrous tissue, which includes degenerate masses of zona pellucida and yolk. (× 64.)

Fig. 2. Medullary lacunae of *Echidna* ovary, containing extensive haemorrhage from large ruptured follicle. Blood pigment is seen in yolk-ingesting phagocytes. (× 148.)

THE FORMATION OF THE CONNECTING STALK AND THE EXTENSION OF THE AMNIOTIC CAVITY TOWARDS THE TISSUE OF THE CONNECTING STALK IN YOUNG HUMAN EMBRYOS

By J. FLORIAN, M.D.

Masaryk University, Brno

From the Department of Anatomy and Embryology, University College, London

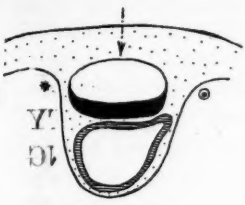
V. Möllendorff first drew attention to the relation of the ectoderm to the mesoderm of the stalk in very young human embryos; in the description of the embryo OP (1921) he describes a "Zerfallende Epithelwucherung des Amnions" (1921, pp. 416, 417; fig. 9, p. 415) behind the caudal end of the embryonic plate, in which the epithelium degenerates and so the amniotic cavity is enlarged at its cost.

In the course of the study of a number of young human embryos I have had the opportunity of convincing myself of the correctness of the above-mentioned discovery, and shall now try to give a description of my own observations.

In the Fetzer embryo, the detailed description of which I shall shortly publish in collaboration with Dr Fetzer, as well as in the embryo Bi I (Florian, 1927) and T.F. (Florian, 1927, 1928 *b*) I was able to observe, in the neighbourhood of the tip of the amnion, granules in the mesoderm which can only be interpreted as the result of the dissolution of tissue proving the correctness of v. Möllendorff's observation. In the embryo Bi II, I shall describe the region in question in detail; in the present paper I shall occupy myself only with the description of the relations between the stalk ectoderm (I use this name in contradistinction to the amniotic ectoderm of which it is the direct continuation) and the stalk mesoderm in the embryo Bi II (with four paired somites) and Bi XI (with ten paired somites). The stalk ectoderm is separated from the ectoderm of the embryonal disc by the cloacal membrane; it will, therefore, also be necessary to take into consideration the surroundings of the cloacal membrane in our description.

In order that the reader may be able to follow my observations more easily, I shall begin with a short description of the early development of the human embryo and its connecting stalk.

Stage 1 (text-fig. 1) corresponds with the Peters embryo (1899; Grosser, 1913): the primitive streak primordium and the stalk are not yet present; the embryo is situated in a thickening of the chorionic mesoderm. The future



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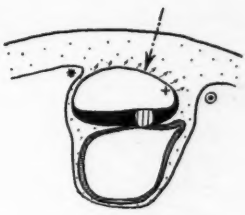

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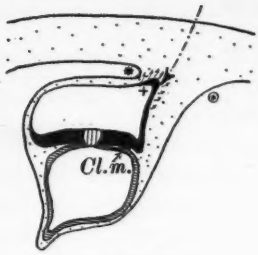

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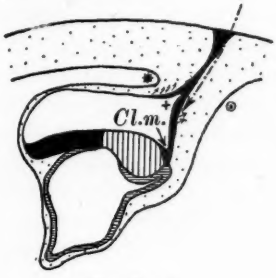

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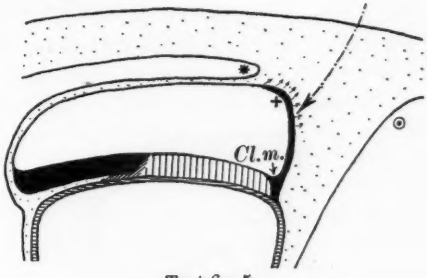

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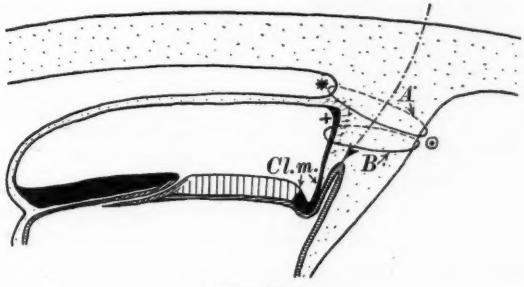
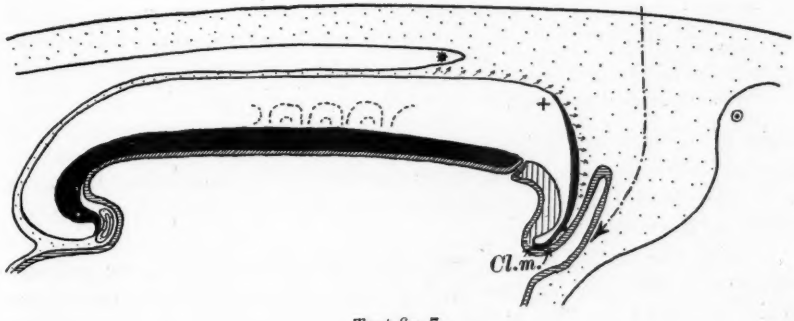
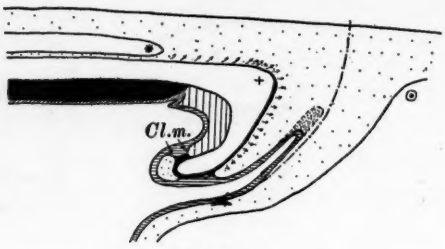


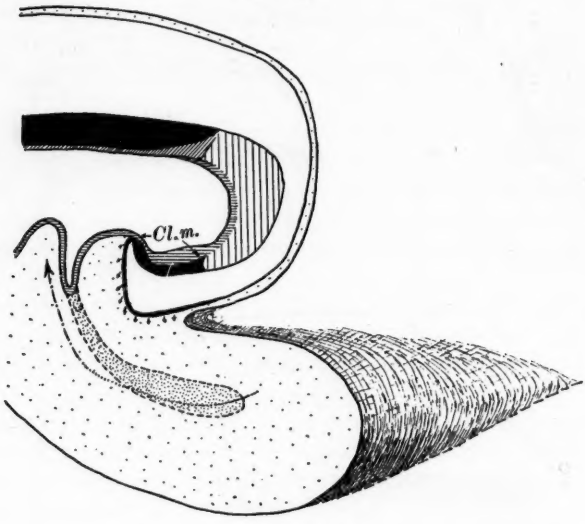
Text-fig. 6



Text-fig. 7



Text-fig. 8



Text-fig. 9

Text-figs. 1–9. Schemes of the chief stages in the development of the human embryo (pp. 454–61). Ectoderm black; entoderm lined horizontally, primitive streak vertically, head process and chorda plate obliquely. Mesoderm dotted. The axis of the connecting stalk is marked by an arrow. The limits of the connecting stalk are marked by ∗ and ⊙, the limits of the umbilical stalk by + and ⊙. The direction of the extension of the amniotic cavity towards the connecting stalk is marked by arrows. The parts of the allantois and of the axis of the connecting stalk situated out of the median plane are finely dotted. *A*. Connecting stalk; *B*. umbilical stalk; *Cl.m.* cloacal membrane.

limits of the stalk are designated by a ⊙ and a ∗. The axis of that part of the chorionic mesoderm, which will be transformed into the stalk in the course of further development, is marked by an arrow: it is perpendicular to the middle of the embryonal plate.

During the further development, the amniotic cavity and the yolk-sac enlarge so rapidly that the mesoderm covering them is not able to keep pace. Whilst in stage 1 (text-fig. 1) the mesoderm of the amnion and that covering

the dorsal marginal part of the yolk-sac are similar in structure to the chorionic mesoderm, in stage 2 (text-fig. 2) the mesoderm covering the whole yolk-sac and the cranial end of the amniotic cavity has taken on a different structure, and is becoming transformed into a "mesothelium." The cells of the mesoderm in this region are connected with the cells of the amniotic ectoderm and with those of the yolk-sac entoderm by means of cytodesmata, and some of the cells of the yolk-sac entoderm appear to have entered the mesoderm. The transition of the mesodermal layer which covers the cranial end of the amnion into the chorionic mesoderm (text-fig. 2*) represents the cranial limit of the connecting stalk, which first begins to be formed in this stage. The first traces of the stalk appear, therefore, in the stage when the primitive streak primordium is represented by a localised fusion of the embryonal ectoderm with the entoderm of the yolk-sac (embryo OP v. Möllendorff). The yolk-sac (in this stage) runs out towards the connecting stalk in the form of a slight diverticulum. Already in this stage v. Möllendorff described (1921, 1925) an active extension of the amniotic cavity towards the stalk tissue (in a dorsal and caudal direction from the embryonal plate). If we regard the caudal limit of the connecting stalk (⊙ in text-figs. 1–8) as a fixed point, we may say that the embryonal plate grows in the cranial direction, while the amniotic cavity expands caudally and dorsally. The yolk-sac correspondingly grows forwards below the embryonic plate almost up to the cranial end of the latter, and also grows in the caudal direction. Its growth in this direction, however, encounters the resistance of the connecting stalk tissue and so, not being able to extend freely, it grows towards the connecting stalk in the form of a diverticulum.

Already in this stage we can distinguish two parts in the connecting stalk which I propose to term the amnio-embryonal stalk and the umbilical stalk respectively. The amnio-embryonal stalk (between ⊙ and * in text-figs. 1–8) attaches the embryonal formation (amnio-embryonal and yolk-sac vesicles) as a whole to the chorionic mesoderm and continues on the one hand into the amniotic mesoderm, and on the other into the umbilical stalk.

The umbilical stalk (between + and ⊙ in text-figs. 2–8) represents a partial continuation of the amnio-embryonal stalk; on its cranial surface it is covered by the stalk ectoderm which is continuous with the ectoderm of the embryonic plate and with that of the amnion, and its whole surface can only be seen if the amnion is opened up. The most important difference between the amnio-embryonal stalk and the umbilical stalk lies in the fact that the latter is in all stages covered on its cranial surface by ectoderm and that it is transformed into the umbilical cord during later stages of development. The amnio-embryonal stalk on the other hand persists for a time but finally disappears when the amniotic mesoderm fuses with that of the chorion.

The axis of the connecting stalk (marked by an arrow) begins already in stage 2 (text-fig. 2) to form an acute angle (open caudally) with the embryonic plate and has moved slightly towards the caudal end of the embryo.

In stage 3 (text-fig. 3, corresponding approximately with the Fetzer embryo (Fetzer-Florian, 1929)) both the amnio-embryonal and the umbilical stalks are quite distinct. The axis of the connecting stalk has now come to lie behind the caudal end of the embryonic plate and it is beginning to form a curve with the convexity directed caudally. The amniotic cavity runs out into a distinct amniotic tip caudally and dorsally, a feature which is to be seen in all following stages. The extension of the amniotic cavity towards the tissue of the connecting stalk takes place in an opposite direction to that of the embryonic plate, the result being, that the distance between the amniotic tip on the one hand and the chorionic ectoderm and the caudal limit of the amnio-embryonal stalk on the other increases at a much slower rate than the distance between the cranial end of the embryonic plate and the above-mentioned structures.

In this stage, approximately in the middle of the embryonic plate, there is present a distinct primordium of the primitive streak and, close to the caudal end of the plate, the cloacal membrane is already developed. It is noteworthy that these two structures are in no way connected in their origin in the human embryo. The primitive streak primordium seems to correspond in its position with Hensen's knot. In this stage, the yolk-sac does not send any distinct diverticulum towards the stalk.

In stage 4, represented by the embryo Bi I, of which a schema is shown in text-fig. 4, the bending of the axis of the stalk has become more distinct, and its tip forms a sharper angle with the embryonic plate than in the preceding stage. In text-fig. 4 I have shown an amniotic duct connecting the amniotic ectoderm with the chorionic ectoderm, because two human embryos (Bi I, Florian, 1927 and Strahl-Beneke, 1910) belonging to this stage possess it. It is not certain whether it is only a chance that the amniotic duct is not present in the embryos represented by text-figs. 1–3. The knot which represented the primitive streak primordium in the preceding two stages has now become transformed into a true "streak," at the end of which there is a distinct "end-knot of the primitive streak." The thickened end-knot produces a ventral down-bulging of the underlying wall of the yolk-sac and so a diverticulum is produced, at the caudal end of which the cloacal membrane is situated. This diverticulum resembles an allantoic outgrowth—with which, however, it has nothing to do, because it disappears during the later development by opening out into the yolk-sac cavity (Florian-Völker, 1929).

In stage 5 (text-fig. 5, corresponding approximately with the Stieve embryo "Hugo," 1926) the tip of the bent axis of the stalk has passed still further caudally. The primitive streak occupies the whole caudal half of the embryonic plate and the primordium of the head process has appeared. The end-knot of the primitive streak has disappeared, and the above-mentioned caudal diverticulum has become merged in the yolk-sac cavity.

In stage 6 (text-fig. 6, corresponding approximately with the embryo Peh.$_1$-Hochstetter, Rossenbeck, 1923) a new diverticulum is seen extending almost vertically upwards from the caudo-dorsal extremity of the yolk-sac

into the stalk mesoderm. I propose to speak of this as the allanto-enteric diverticulum since its proximal part represents the later hind-gut, its distal portion the entodermal allantoic canal. The proximal part coincides in position with the cloacal membrane, furnishing its entodermal layer, whilst the allantoic canal is situated caudally to that membrane. The allanto-enteric diverticulum in this stage appears at first sight to be very similar to the diverticulum described in stage 4, which has been regarded by many authors, including myself, as the allantoic primordium, but there is a very important difference between the two, apart from the fact that the one is transitory, the other permanent. The cloacal membrane is situated in stage 4 at the end of the diverticulum there present, but in stage 6 it lies at the opening of the diverticulum into the yolk-sac cavity. The part of the diverticulum caudal to the cloacal membrane (the above-mentioned "allantoic" canal) is, therefore, in stage 4 not yet present. The axis of the stalk is now situated caudally to the amniotic cavity and its tip is directed to the upper or caudal end of the allantoic canal.

In stage 7 (text-fig. 7, corresponding approximately with the embryo Bi II) the axis of the stalk lies still more caudally, being now situated behind the allanto-enteric diverticulum. The cloacal membrane is divided into two parts: one of them lies at the orifice of the diverticulum, the other is situated more caudally.

In stage 8 (text-fig. 8, corresponding approximately with the Sternberg embryo (1927 *a*), with four paired somites) the cranial part of the cloacal membrane is situated in the now very distinct primordium of the hind-gut. The other part lies close behind the orifice of the allanto-enteric diverticulum into the yolk-sac; it is now in process of degeneration and has become separated into three pieces. Whereas in stage 7, the allanto-enteric diverticulum lies wholly in the median plane of the embryo, in this stage the lengthening of the stalk has permitted a slight rotation of the embryo around its long axis, with the result that the end of the allantoic canal is no longer in the median plane. The mesoderm between the allantoic canal and the stalk ectoderm is now much thicker than in the preceding stage. The axis of the stalk now makes such a sharp curve that its tip runs nearly parallel to the long axis of the embryo.

In stage 9 (text-fig. 9, embryo Bi XI with ten paired somites) certain important advances have been made in the region under discussion, (*a*) the caudal end of the embryo now projects freely backwards as the result of the developmental processes already initiated in stage 7, (*b*) the connecting stalk has increased greatly in length and, as the result of the growth of the tail-end of the embryo and the development of the hind-gut, has been carried ventrally so that it now arises from the ventral side of the embryo, in front of the freely projecting caudal end of the latter, (*c*) as the result of the lengthening of the stalk, the embryo has turned its right side towards the chorion, (*d*) the opening of the allantoic canal is now situated on the floor of the hind-gut. The tip of

the axis of the connecting stalk is once more perpendicular to the axis of the embryonic body, but it has made a rotation of 180° in comparison with the stage 1. We can see, therefore, that *the migration of the insertion of the umbilical stalk from the dorsal-caudal to the ventral aspect of the body of the embryo is the result partly of the active growth of the stalk and partly of the growth of the tail-end of the embryo in the caudal direction and the correlated extension of the amniotic cavity in the same direction.* We see further that the embryo need not change its position during this process. The definitive cloacal membrane is now established in the floor of the hind-gut. It is formed by the cranial part of the cloacal membrane of stages 7 and 8. The whole allantoic diverticulum of this stage corresponds to that part of the allanto-enteric diverticulum in stage 7 which is situated behind the definitive cloacal membrane. Only the part of the allantoic diverticulum which is situated close to its opening into the hind-gut is situated in the median plane as the result of the rotation of the embryonic body round its long axis.

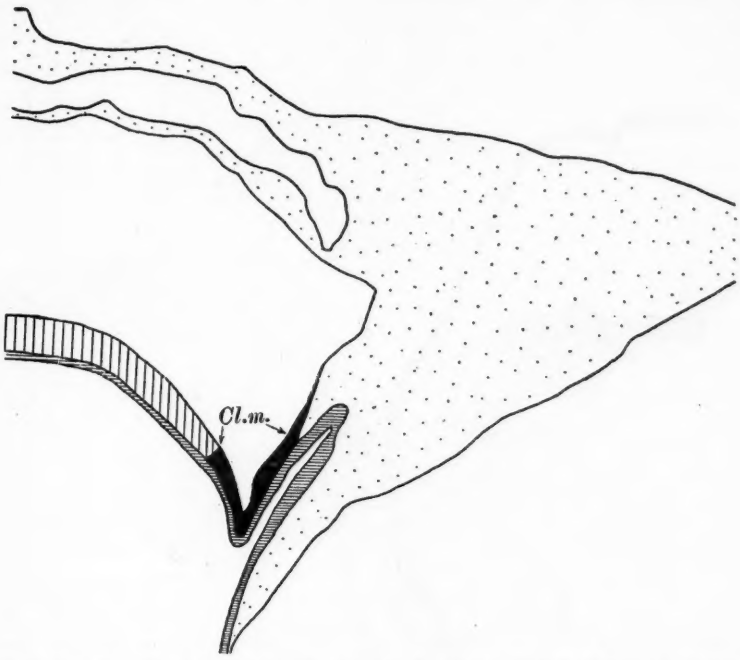
If we compare the cloacal membrane in text-figs. 7 and 8, we notice that the definitive part of the cloacal membrane is situated in stage 7 (text-fig. 7)—and the same is true for stage 6 (text-fig. 6)—partly in the allanto-enteric diverticulum, but in stage 8 (text-fig. 8) the definitive cloacal membrane is now situated in the hind-gut. This fact justifies the conclusion that the part of the allanto-enteric diverticulum close to its opening into the yolk-sac really belongs not to the allantois, but to the hind-gut. In this connection I call attention to the characters of the entoderm in this region of the embryonic body (p. 467), which support my interpretation. If that interpretation is correct, it is clear that we cannot determine with certainty the cranial limit of the allantoic canal in stages prior to stage 8. This is one of the most remarkable differences between the development of the Man (and no doubt that of all the higher Primates) and the development of lower Mammals, and it is conditioned by the presence of the connecting stalk and the very early differentiation of the primordia of the cloacal membrane and the allantois. Only when the insertion of the umbilical stalk to the ventral part of the embryonic body (stage 9, text-fig. 9) is attained and the hind-gut is formed can the human embryo, with regard to the cloacal membrane and the allantois, be compared with that of a lower Mammal.

Now I shall try to support my views by an account of my own observations.

I shall begin my remarks with the description of the cloacal membrane in the Embryo Bi II, in which I have previously described the chorda canal (1928 *a*). The embryo was cut cranio-caudally. The graphic reconstruction of the caudal end of this embryo (text-fig. 11) shows that the hind-gut is already forming, but is still very shallow. The cloacal membrane is not found in this hind-gut primordium, but in that region where the yolk-sac passes into the allanto-enteric diverticulum, the greater part of which corresponds with the allantois of later stages. Caudally to the true cloacal membrane I found a

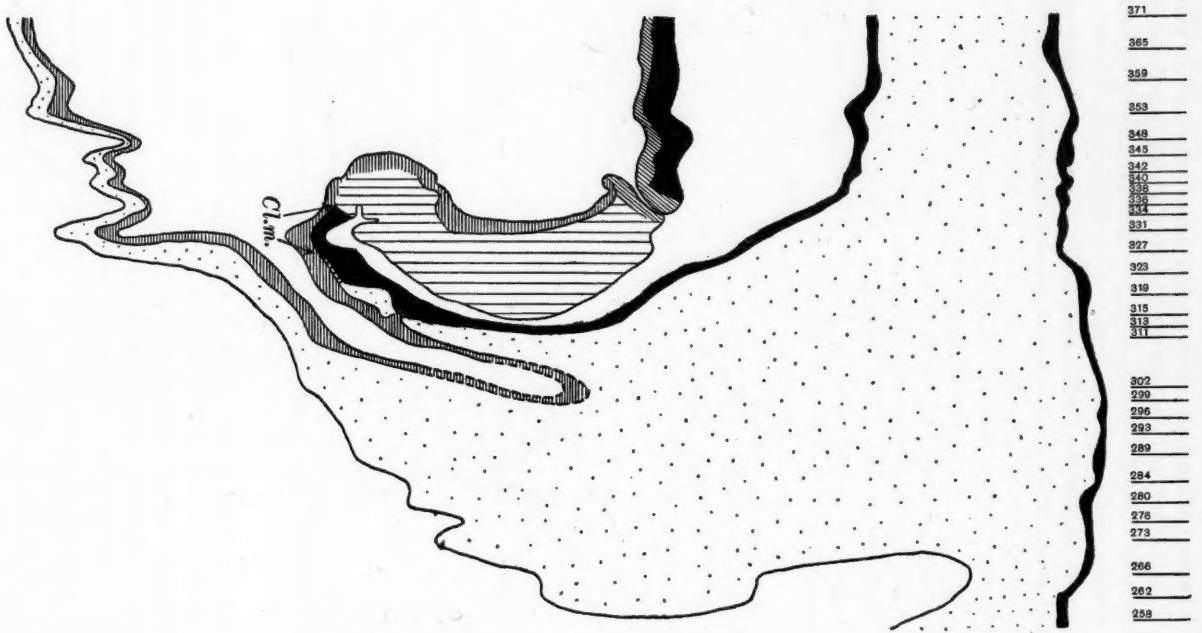
connection between the amniotic ectoderm and the entoderm of the allantoenteric diverticulum (between sections 315 and 314), the significance of which I shall discuss later. Here I wish only to call attention to the region between the cloacal membrane and this connection.

In this region, the embryo Bi II shows nearly the same relations as the Sternberg embryo (1927 *a*), with which it agrees in the number of somites.



Text-fig. 10. Embryo Peh.$_1$-Hochstetter (Rossenbeck, 1923) according to Sternberg (1927 *b*). ×113. Ectoderm black; entoderm lined horizontally, primitive streak vertically. Mesoderm dotted.

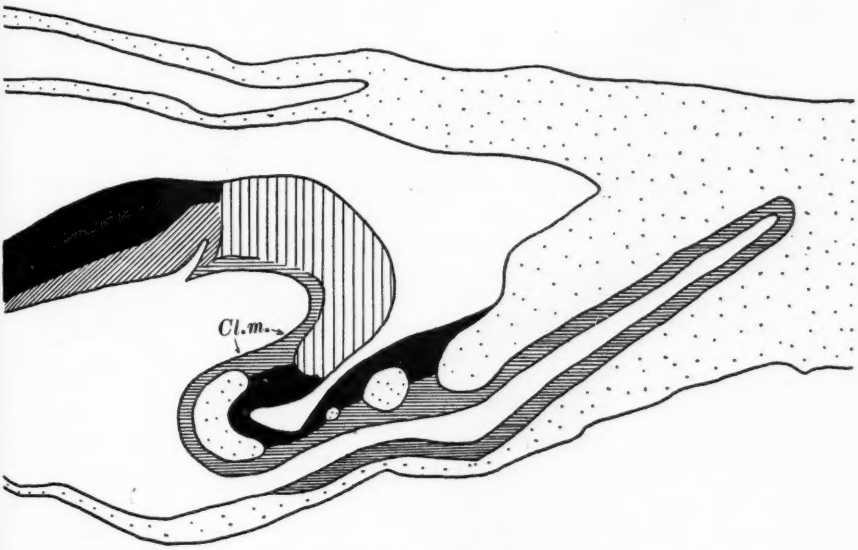
Sternberg has described in his specimen (text-fig. 12) behind the cloacal membrane (which is found in the hind-gut) three separate connections between the amniotic ectoderm and the entoderm of the allantois, and has regarded these as the remains of the original cloacal membrane. I suggested in 1929 (Florian and Völker) the possibility that these connections are the result of secondary fusion of the amniotic ectoderm and the entoderm of the allantois, for the reason that the distance of the points of fusion from the actual cloacal membrane in the Sternberg embryo seemed to be much too great but, more recently, I believe that I have found a distinct transitional stage in the graphic reconstruction of the embryo Bi II (text-fig. 11) between the embryo



Text-fig. 11. Embryo Bi(ttmann) II with four paired somites. ×113. Ectoderm black; entoderm lined horizontally, primitive streak vertically, head-process and chorda-plate obliquely. Mesoderm dotted. The outline of that part of the allanto-enteric diverticulum which is not in the median plane is broken. Sectional planes indicated above the figure.

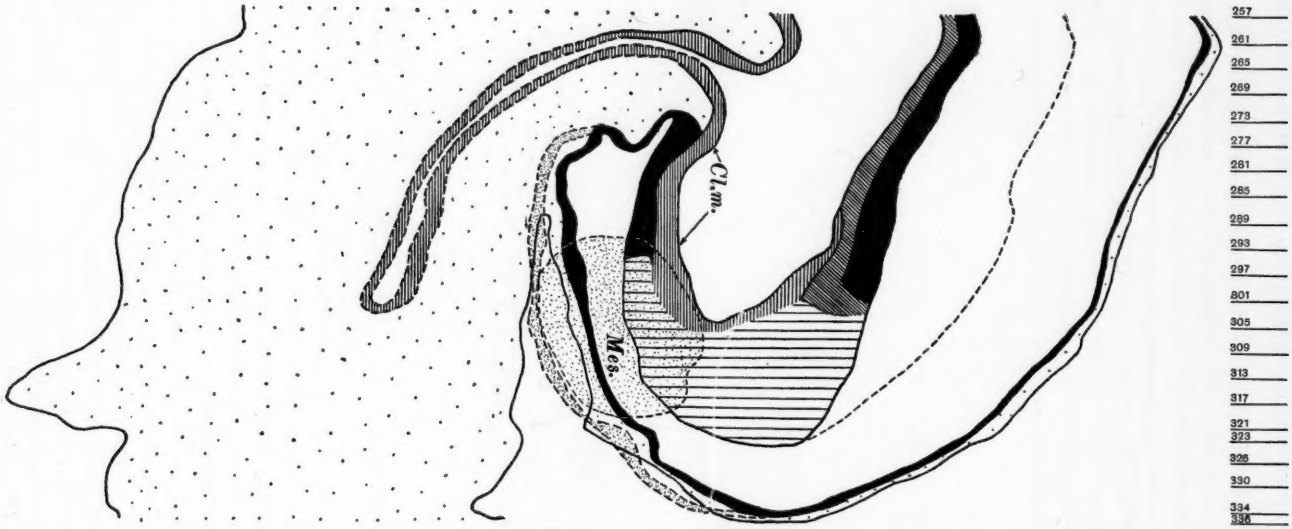
Peh.$_1$-Hochstetter (text-fig. 10) and the Sternberg embryo (text-fig. 12) and accordingly accept the view of Sternberg that they are actually remnants of the original much more extensive cloacal membrane.

In the region between the actual cloacal membrane and the connection of the amniotic ectoderm and the entoderm of the allantois, the relations between the embryonal layers are very difficult to study, although the tissue is well preserved and the embryonal layers can be easily distinguished elsewhere. I, therefore, think it is necessary to describe this region somewhat more in detail.



Text-fig. 12. Embryo Sternberg (1927 *a*, *b*). × 113. Ectoderm black, entoderm lined horizontally, primitive streak, vertically, head-process and chorda-plate, obliquely. Mesoderm dotted.

In section 330 (Plate I, fig. 1) the cloacal membrane has its typical form; it is sharply separated from the mesoderm by a fairly broad space. The various sized granules stained with haematoxylin, which are to be observed in great number in section 229 and which are possibly to be interpreted as a sign of cell destruction, are here present only in minimal quantities. We can accordingly describe this section as the most caudal in which the cloacal membrane shows no noticeable sign of degeneration. In the next (in the caudal direction) section (No. 229) the tissue composing the cloacal membrane seems to be much less compact, especially close to the ectoderm. (It seems that we can see here the limit between the ectodermal and entodermal part of the cloacal membrane, which was not possible in section 330.) In the entodermal part of the cloacal membrane there is a cavity filled with variously sized granules; these



Text-fig. 13. Embryo Bi(ttmann) XI with ten paired somites. ×113. Ectoderm of that part of the amnion not in the median plane finely dotted and its outline indicated by interrupted lines; the sequestered mesoderm mass lying free in the amniotic fluid indicated in the same way. Otherwise as in text-fig. 12.

granules contain enclosures stained with haematoxylin. They are possibly products of cell dissolution. On the right the cloacal membrane is separated from the mesoderm by a wide space; on the left, on the contrary, the mesoderm approaches much nearer to the cloacal membrane and is connected to it by fine but quite distinct cytodesmata. In the next section (328) the ectoderm and the entoderm are connected by a single cell in the region of the cloacal membrane. Otherwise the ectoderm is separated from the entoderm by a distinct space, which is bridged over by fine cytodesmata. The granules referred to as products of cell dissolution are only visible in the entoderm. On the left, the mesoderm is quite near to the cloacal membrane, but one can easily distinguish it from the cloacal membrane. In the next section (327, Plate I, fig. 2) the ectoderm shows a fairly wide connection with the entoderm—we have, therefore, before us a distinct cloacal membrane—but if we compare this section with the section 330, we can note certain differences. The dorsal surface of the cloacal membrane is not flat as in section 330, but shows a distinct pit, whilst its left border is much less distinct than the right, because the mesoderm approaches very close to the cloacal membrane. Products of cell dissolution are not to be observed in the cloacal membrane, but they seem to be present in the mesoderm at a certain distance from it. In section 326 (Plate I, fig. 3) the relations of the embryonal layers are very indistinct. We can observe a cell cord which seems to connect the entoderm and the ectoderm, but the limit between this and the mesoderm is so indistinct that it can scarcely be compared with the well-developed cloacal membrane seen in section 330 (Plate I, fig. 1). Degeneration products are not visible in the cloacal membrane, but they are quite distinct in the mesoderm (on the left). In section 325 (Plate I, fig. 4) the limits between the cloacal membrane and the mesoderm are not much more distinct than in section 326, whilst degeneration products are very clearly visible in the ectoderm near to the amniotic cavity. In section 324 the limits of the cloacal membrane are not more distinct, and there are present in it very many degeneration granules. In section 323 the ectoderm sends out towards the entoderm a narrow cell cord, between the end of which and the entoderm a degenerated cell is present. In section 322 this cell cord nearly reaches the entoderm; a very narrow space, possibly an artefact, lying between the two. On the left of this cell cord, the ectoderm is thickened and the limit towards the mesoderm is very indistinct. In section 321 (Plate I, fig. 5) there are only very indistinct traces of the above-mentioned cell cord. On the left the ectoderm is again thickened as in sections 324–2, and contains numerous granules. The limit between the ectoderm and the mesoderm in this section is non-existent. In the following sections (in the caudal direction) there is no cell cord visible. The above-mentioned thickening of the ectoderm comes to occupy its position and assumes a triangular form; it contains many granules and its limit towards the mesoderm is indistinct. In section 316 the tip of this triangular thickening passes into a very distinct cell cord containing granules. These latter are especially distinct in section 315 (Plate I, fig. 6)

in a narrow cord which can be traced from the ectoderm towards the entoderm. Already in this section, but still more distinctly in section 314 (Plate I, fig. 7), the entoderm sends out a pointed process towards the ectoderm, which is very likely connected with the ectodermic cell cord seen in section 315 and which, as indicated above, shows distinct signs of degeneration. (Similar signs of degeneration are also to be seen in degenerating amniotic ducts.)

In order to understand the development of the hind-gut, it is of importance to know the conditions at the cranial end of the cloacal membrane. The cloacal membrane shows no signs of degeneration in the cranial direction up to section 332. In section 333 a cloacal membrane is still present, but in its centre there is an oval cavity containing numerous granules, staining similarly to those in the caudal region of the membrane. In section 334 the latter is much narrower than in the preceding section. The hinder end of the amniotic cavity extends as a narrow horse-shoe shaped diverticulum ventral to the caudal end of the embryo, immediately in front of the cloacal membrane. The ectoderm in this section is distinct and is separated from the mesoderm, except over a very narrow region in the middle line, where these two layers are fused; we have to do here with the caudal end of the primitive streak, which streak is still to be seen also in section 335. The amniotic cavity is still present in this section, but appears as two separated clefts, representing the continuation of the limbs of the horse-shoe shaped diverticulum in the preceding section. The ectoderm and entoderm are connected in the middle line by a cell mass, in which are present numerous granules, so that we have here the cranial extremity of the cloacal membrane, but the ectoderm is very indistinct, because it is fused dorsally with the mesoderm of the primitive streak and ventrally with the entoderm in the region of the cloacal membrane. In section 336 (Plate II, fig. 11) we find the same relations, but there are no granules in the cloacal membrane. In section 337 the amniotic cavity is still present as a single small, but sharply limited cleft. The ectoderm is quite indistinct. In section 338 (Plate II, fig. 12) neither an amniotic cavity nor the ectoderm can be distinguished. The entoderm is here fused with what is certainly the mesoderm of the primitive streak. In the mesoderm, close to the entoderm, there are present granules of variable size. In section 339 the entoderm of the hind-gut is also fused with the primitive streak mesoderm.

The observations recorded above justify us in drawing the following conclusions: the cloacal membrane shows very distinct signs of degeneration over a considerable extent of its caudal region. Products of cell dissolution are also present in the cranial region of the cloacal membrane, but they are here much less abundant than in its caudal end. At its cranial end the cloacal membrane passes over without any limit into the primitive streak. Cranial to the cloacal membrane the mesoderm is in continuity with both the ectoderm and the entoderm and a migration of cells from the entoderm into the mesoderm seems to be very probable in several places.

In this connection we would call attention to the form of the entoderm

cells in the neighbourhood of the cloacal membrane. The study of the entoderm in this region is not quite easy, because the entoderm is cut in most places obliquely; nevertheless we can conclude that the entoderm, cranial to the posterior intestinal portal (in the mid-gut as well as in the yolk-sac), consists usually of cubical cells, though in places the cells are flattened. In the posterior intestinal portal and in the hind-gut the entoderm cells assume a higher, even cylindrical form, and their cytoplasm stains deeply. The entoderm of the yolk-sac, elsewhere low, is higher in the region of the cloacal membrane and where the yolk-sac passes over into the allanto-enteric diverticulum. In the most caudal part of the hind-gut the entoderm is lower again, but it cannot be studied easily because of the obliquity of the sectional plane.

The entoderm is especially high in the caudal part of the cloacal membrane, where there are signs of the degeneration of the cloacal membrane. In the ventral part of the orifice of the allanto-enteric diverticulum the entoderm contains numerous granules.

The above-mentioned allanto-enteric diverticulum of the yolk-sac has in transverse section a circular outline near its opening into the yolk-sac. Caudally to section 322 it is oval with its long axis running dorso-ventrally. Starting from this section, the entodermal cells in the ventral wall of the diverticulum contain small basally situated vacuoles; the nuclei lie towards the free surfaces of the cells where the cytoplasm stains deeply like that of the cells in the dorsal wall of the diverticulum. Caudally the cavity of the allanto-enteric diverticulum assumes an elongated oval form (Plate I, fig. 7); the basal vacuoles appear also in the cells of the dorsal wall. In this caudal region of the allanto-enteric diverticulum, the cells become reduced in height. The form of the entoderm cells in the caudal region of the allanto-enteric diverticulum of embryo Bi II corresponds with that of the cells over the whole extent of the allantois in embryo Bi XI (Plate II, figs. 9, 10).

The significance of these observations I have discussed above (p. 460); now we may pass to the description of the cloacal membrane in embryo Bi XI.

The embryo Bi(ttmann) XI, of whose caudal end a graphic reconstruction is shown in text-fig. 13, was obtained by an operation by Dr O. Bittmann in Brno and was fixed intact in the chorionic vesicle in Zenker's solution immediately after the operation. About four hours later the chorionic vesicle was carefully opened. The specimen was imbedded in paraffin and cut nearly transversely in the cranio-caudal direction (the sections are 7μ thick). The entire embryo is well preserved and without any deformation; it possesses ten paired somites. I intend to describe it in detail later, and now I shall direct attention only to the cloacal membrane and the relations between the ectoderm and the mesoderm of the stalk.

The cranial end of the cloacal membrane is in embryo Bi XI indicated already in section 272, where there is no mesoderm between the ectoderm and the entoderm in the median plane and the ectoderm nearly reaches the entoderm. In sections 273 and 274 a triangular process of the ectoderm meets

the entoderm and fusion of the two layers has probably been effected. But the cloacal membrane is quite definitely formed in section 276. There are no granules regarded as products of cell dissolution to be observed in sections 276 to 279, and no other signs of degeneration of the cloacal membrane are present. Here and there in the cranial end of the cloacal membrane the ectoderm is loosened from the entoderm, but such places are always very small, and they are also to be seen in mid-region of the membrane and accordingly are not to be regarded as indications of degeneration of the membrane. In section 280 cell granules first appear, but they are always very few in number and much smaller than those in embryo Bi II.

The cloacal membrane can be followed up to section 294 without any difficulty (in section 293 there is a mitosis in one of its cells). In section 295 the cloacal membrane is much more indistinct than in the preceding section, because the mesoderm on both sides comes close up to it and the area of fusion of the ectoderm and entoderm is greatly reduced. In the following section there is a cell mass which connects the ectoderm and entoderm, but its cells seem to belong to the mesoderm; we have, therefore, reached the transition region where the cloacal membrane passes into the primitive streak. From the cloacal membrane up to the head-process the three embryonal layers are in continuity with each other in the median plane.

It is not necessary here to enter into detailed comparison of the condition of the cloacal membrane in my specimens with that described in other human embryos. I need only refer the reader to the paper by Florian-Völker, 1929, in which the cloacal membrane in other very young human embryos is described, and the papers of Sternberg (1927 *a*, 1927 *b*). It would be superfluous to repeat the details here.

Before I proceed to discuss the significance of my observations, I shall describe the conditions behind the cloacal membrane and, more particularly, the relations between the ectoderm and mesoderm of the connecting stalk in both my specimens, beginning with the embryo Bi II. In this embryo the interpretation of the sections is made difficult by the obliquity of the sectional plane. The result of this is that the limit between the ectoderm and mesoderm is in some places obliterated. But it seems very probable that the indistinct limit of the mentioned layers is not simply the result of the mentioned obliquity, but that there is actually no distinct limit between them. The ectoderm of the stalk consists of a layer of flattened or low cubical cells, which exhibits only rarely a distinct limit towards the mesoderm and, even in these places, the ectodermal cells are connected with the mesodermal by means of numerous fine cytodesmata. We may divide the stalk into two regions: a ventral one extending to the level of the caudal end of the allantois, and a dorsal one found dorsally to the latter.

I shall describe the ventral region of the stalk first. In many places the stalk epithelium consists here of three or more cell layers, of which the cells of the basal layer are connected with the underlying mesodermal cells by

means of processes. It is impossible to prove to which germ layer the single cells of this epithelium belong. One possibility is that we have here to do with an ectoderm consisting of many cell layers, and that the cells of the basal layer are connected with the mesodermal cells; in several places the axes of these basal cells are so directed as to suggest the passage of ectodermic cells into the mesoderm. But there is also another possibility: the cells of the basal layer may belong to the mesoderm, although they are so closely related to the ectoderm. It is especially difficult to find the limit between the ectoderm and mesoderm close to the median plane in the region between the ectoderm and the allanto-enteric diverticulum, as was mentioned in the description of the cloacal membrane. We can see this region (close to the median plane) on the right of fig. 8 (Plate I). On the left of the same figure there is a cell to be seen, which seems to belong to the stalk ectoderm and which is connected by means of a very long and distinct process with the mesodermal cells (Plate I, fig. 8 +).

As we have mentioned above, the indistinct limit between the ectoderm and the mesoderm in this region is not only a result of the oblique plane of sections; it is very possible that some of the ectodermal cells pass into the mesoderm.

Also in the dorsal part of the connecting stalk (dorsal to the level of the caudal end of the allanto-enteric diverticulum) the limit between the ectoderm and the mesoderm is very indistinct. The amniotic ectoderm close to the insertion of the amnion into the connecting stalk is distinguishable by its characters; whilst the amniotic ectoderm far from that insertion consists of a single layer of very flattened cells, the amniotic ectoderm close to its transition into the stalk ectoderm is formed by several layers. Its basal layer represents the direct continuation of the amniotic ectoderm of that part of the amnion remote from the insertion on the connecting stalk, and consists of a single, continuous layer of cells which has stained very deeply with eosin. The cells are cubical and their limits are very distinct. On this basal layer are situated polygonal or round cells whose cytoplasm has stained only faintly with haematoxylin. In their cytoplasm there are distinct vacuoles especially close to the cell surface next the amniotic cavity. These cells are rather large and contain a large, round nucleus, which is larger and rounder than the nuclei of the basal layer. These cells are very often separated from each other by distinct spaces, and accordingly they do not form a continuous layer. The connection of the cells of this layer with the cells of the basal layer is in some places only very loose, and there is no doubt that they can be shed into the amniotic cavity where they undergo dissolution. The products of this cell dissolution can very easily be found in the amniotic cavity.

The two above-mentioned cell layers of the amniotic ectoderm can be followed into the stalk ectoderm. The upper layer of the stalk ectoderm shows no particular differences as compared with the amnion in its neighbourhood, but the cells of the basal layer (deeply stained with eosin) enter into very complicated relations with the surrounding mesoderm. The form of cells of

the basal layer is very irregular: some of them are cubical like the cells in the basal layer of the amnion, and there are many transitions between them and the upper layer of the stalk ectoderm; it seems to be very likely that these cells will be shed into the amniotic cavity during the further development, and there dissolved.

The other cells in the basal layer retain their eosinophil character. Close to the insertion of the amnion into the connecting stalk, these cells send out long and broad processes into the mesoderm and, as the result, they present peculiar forms and their nuclei become oval (Plate II, fig. 14). In the tissue close to the ectoderm there are in some places very distinct granules (Plate II, fig. 15). These seem to be a certain proof of the extension of the amniotic cavity at the expense of the stalk mesoderm; the ectoderm grows here deeply into the mesoderm and compresses it or brings about its dissolution. In this way the amniotic cavity is enlarged towards the tissue of the connecting stalk, this enlargement being specially marked and proceeding most rapidly close to the insertion of the amnion into the connecting stalk. The convex outline of the surface of the connecting stalk directed towards the amniotic cavity (in the sections) is the result of this process (Plate II, figs. 13 and 16).

Even in the region remote from the insertion of the amnion into the connecting stalk there are present, underneath the stalk ectoderm, products of cell dissolution, so that even here the mesoderm undergoes an involution. The form of the ectoderm also differs very much in this same region from that close to the insertion (Plate III, fig. 17). The ectodermal cells are in places very flattened (like an endothelium) and vaulted towards the amniotic cavity so that the axis of the cell forms here a curve convex towards the amniotic cavity. Even in this region there is evidence that some of the ectodermal cells are eliminated into the amniotic cavity and dissolved. Such cells contain, even before they are eliminated, large vacuoles and their cytoplasm stains only with haematoxylin. It is of some interest that also the mesodermal cells close underneath the ectoderm contain vacuoles.

In this same region there are other places where it is impossible to prove the existence of an ectodermal layer, the mesoderm alone appearing to bound the amniotic cavity. Such places are in the embryo Bi II never very large. In other places the ectoderm is very distinct; its cells are very deeply stained with eosin in contrast to the mesodermal cells, but the limit between the ectoderm and the mesoderm is not distinct, since the cells of the former are connected with those of the latter by means of cytodesmata.

(In section 332 I happened to find a cell in the mesoderm which was much larger than the surrounding mesodermal cells, and deeply stained with eosin. It seems very likely that we have here to do with an ectodermal cell which has emigrated into the mesoderm.)

We may now pass to the description of the relations between the ectoderm and the mesoderm of the connecting stalk in embryo Bi XI (text-figs. 9, 13).

The flattened amniotic ectoderm in embryo Bi XI passes into the ectoderm

of the connecting stalk, which consists of much higher cells; these cells cannot be shortly designated as cubical or cylindrical, because their form is too irregular and we must, therefore, describe them more in detail.

As in the embryo Bi II, we can, even in the embryo Bi XI, find in the stalk ectoderm cells which are eliminated into the amniotic cavity and dissolved. They appear to lie on a single layer of flattened cells (Plate III, figs. 22 and 23). These flattened cells in some places become higher and assume an irregular form. The line formed by the basal surface of these cells is not rectilinear as in a cubical or cylindrical epithelium, but quite uneven. The reason for this is to be found in the migration, in many places, of some of the ectodermal cells into the mesoderm (through the basal line of the ectoderm). They are to be found in varying stages of passage into the mesoderm (Plate III, fig. 22). We can very often observe cells with half of their bodies below the basal line of the ectoderm and connected with the mesodermal cells by means of wide processes. In one place (Plate III, fig. 21), where the ectoderm forms a comparatively regular layer and where the basal line is rectilinear, we find a cell, with one half of its body situated above the basal line, the other half below it, the two halves being connected by a very narrow bridge. Even the nucleus is divided into two halves connected by a very narrow, but quite distinct, bridge. Just on the right of this cell there is another cell which sends a broad process into the mesoderm, the sharpened end of its nucleus lying below the basal line.

In other places the ectodermal cells form little groups, penetrating into the mesoderm. We can see in Plate III, fig. 18 such a group in the form of a triangle, the base of which lies at the upper surface of the ectoderm, whilst the tip is directed towards the mesoderm. In such a group the cells undergo a dissolution in such a way that finally only those cells remain which cover the mesoderm; the inner cells disappear and in their place there arises a small cavity connected with the amniotic cavity (Plate III, fig. 19). This is one way in which the amniotic cavity is enlarged towards the connecting stalk.

In order to elucidate further the mode of extension of the amniotic cavity towards the stalk mesoderm, I must describe a very interesting observation in embryo Bi XI.

As is to be seen in Plate III, figs. 20 and 24, the right side of the embryo (in the younger embryos it is the dorsal side) is turned towards the chorionic membrane and the insertion of the amnion into the connecting stalk is ventral to, and on the right (in the figure) of, the caudal end of the embryo. The amniotic vesicle runs out towards the mesoderm of the connecting stalk in the form of a wide bay, in which a free cell mass is situated. This cell mass, according to its structure, belongs without any doubt to the mesoderm, but it is completely separated from the stalk mesoderm and lies free in the amniotic fluid. As is to be seen especially in Plate III, fig. 24, the mesodermal cells are comparatively well preserved in the middle of the mass, in contrast to its surface, where no cells are visible. We have here, without any doubt, to do with a mass of mesoderm in course of dissolution, from the surface inwards.

That this is so is indicated by the presence of numerous granules on the whole surface of the mass, and especially in that part of the surface which is turned towards the stalk ectoderm; here—but only here—very slight traces of the ectoderm are present on the surface of the mass which, in some places, touches the stalk ectoderm.

In my opinion we can explain the presence of such a quite separated mesodermal mass in the amniotic cavity and its dissolution only in the following way. The stalk ectoderm penetrates into the mesoderm as above described and brings about its dissolution, where it is in direct contact with it, but it also can grow round a comparatively large mass of mesoderm and separate it completely from its surroundings. Such a sequestered mass remains for a time in the amniotic fluid, until it is completely dissolved. This is another and very intensive way, in which the amniotic cavity increases in extent at the expense of the connecting stalk.

The observations recorded above justify the opinion that the extension of the amniotic cavity first mentioned by v. Möllendorff in the very young embryos OP and WO takes place even in the embryo Bi XI with ten paired somites and that it is even in this much more developed specimen in active progress. A knowledge of the above-mentioned processes is very important for the understanding of the development of the connecting stalk in Man, as I have attempted to describe by means of the schematic median sections (text-figs. 1–9).

In this connection I must make some mention of the literature bearing on this question.

I have already had the opportunity (Florian, 1928 *b*, pp. 537–8) of describing my observations on the stalk ectoderm of some young human embryos. I was then inclined to accept the opinion of Fahrenholz (1927) that the amniotic cavity is not enlarged towards the tissue of the connecting stalk, but that, on the contrary, it grows out of the connecting stalk. But the sequestration of a part of the stalk mesoderm, described in embryo Bi XI, cannot be explained by Fahrenholz's view and, therefore, I am obliged to mention the Fahrenholz's observations more in detail.

Here I cite the most important part of Fahrenholz's account (1927): "Auch bei dem Ei Ho sind die Degenerationserscheinungen im Amnionzipfel nachweisbar. . . . Es lässt sich jedoch in diesem Fall zeigen, dass diese Vorgänge nicht zu einer Erweiterung, sondern umgekehrt zu einer Verkleinerung der Amnionhöhle führen. Das Amnionepithel wächst nicht in den Haftstiel hinein, sondern es zieht sich daraus zurück" (pp. 301–2). "Wir haben hier also einen Hohlraum im Bindegewebe vor uns, der in der Nachbarschaft des Amnionepithels noch gut erhalten, an seinem distalen Ende aber bereits im Schwinden begriffen ist und noch Reste des Amnionepithels enthält, das ihn früher auskleidete. Der Spalt ist über neun Schnitte von 7·5μ Dicke zu verfolgen und reicht stellenweise bis an die Chorionmembran heran. . . . Ich muss der Meinung von *Grosser* (1924) und *Bryce* (1924) beipflichten, dass Amniongang usw. Reste eines primären Zusammenhanges zwischen Amnion-

und Chorionepithel sind. Diese Annahme allein bringt die Befunde unter einen Hut und gibt eine Erklärung nicht nur für den Amnionzipfel, den Amniongang und die Zelldegenerationen, sondern auch für den Amnionnabel und die Choriongänge des Haftstieles, denen gegenüber die v. *Möllendorffs* Theorie versagt. Ein eigentlicher Amniongang fehlt beim Ei Ho. Die Zellen des oben (S. 268) erwähnten Epithelstranges im Haftstiel (Fig. 30 und 31) unterscheiden sich durch ihren hellen, scharf umgrenzten Plasmaleib deutlich von den dunkel gefärbten Zellen des Amnionepithels. Sie gleichen dagegen vollkommen den Elementen der *Langhans*schen Zellschicht. Ich halte den Strang daher für einen Chorionstrang" (p. 303).

The difference between v. Möllendorff's observations on embryos OP (1921) and WO (1925) on the one hand, and Fahrenholz's observations on the other, could possibly be put in this way, that v. Möllendorff studied the stalk ectoderm in that region, where an extension of the amniotic cavity towards the connecting stalk takes place, whilst Fahrenholz devoted particular attention to the place of the insertion of the amniotic duct into the stalk ectoderm. The fact that the epithelial cord, described in embryo Ho by Fahrenholz, consists of Langhan's cells, is not in contradiction with the opinion that we have here to do with the remains of an amniotic duct. I had the opportunity to convince myself in embryo Bi I, where there is a continuous connection between the ectoderm of the chorion and that of the amnion, that the caudal part of the amniotic duct consists of Langhan's cells. Stump (1929) made the same observation in an embryo, in which there is the same continuous connection between the ectoderm of the chorion and the amnion, but which is much older than the embryo Bi I; it is the oldest embryo in which such a continuous connection has been described. I believe, therefore, that the "chorionic duct" described by Fahrenholz in embryo Ho represents remains of an amniotic duct, and that Fahrenholz was dealing with the junction of the amniotic duct with the stalk ectoderm.

v. Möllendorff's opinion possibly does not explain the amniotic duct so well as Fahrenholz's view, but there are, I believe, other and more important difficulties raised by the view of Fahrenholz: it is not able, for example, to explain our observations on the stalk ectoderm of the embryo Bi II and Bi XI. We ought to count also on the possibility of a combination of an involution of the amniotic cavity in the neighbourhood of the insertion of the amniotic duct and of an extension of the same in other parts of the stalk ectoderm.

I may cite here another important observation made by Rossenbeck in the embryo Peh.$_1$-Hochstetter (1923, p. 353): "Auffallend ist, dass fünf Schnitte vor dem caudalen Ende der Amnionhöhle ihre dorsale Wand wie zersprengt erscheint, so dass man den Eindruck hat, als würde sie hier direkt von dem Mesoblastgewebe des Bauchstieles begrenzt (vgl. Taf. XLI, Abb. 46)." I have already described places (p. 460) in the embryo Bi II, where there is also no ectoderm visible, but this region in the embryo Peh.$_1$-Hochstetter seems to be much larger. In this connection I call attention to the outline

of the connecting stalk towards the amniotic cavity in the sections of embryo Peh.$_1$-Hochstetter; it is convex towards the amniotic cavity as it is also in the embryo Bi II. We could easily imagine that the stalk ectoderm could grow round and isolate a part of the stalk mesoderm with resulting sequestration of the latter during the further development.

If we compare the early development of the Man with the development of the other Mammals on the basis of the observations and interpretations set forth in the preceding pages, we reach the following conclusions:

The most remarkable difference—the reason of all later-mentioned differences—between the development of Man and that of other Mammals, is to be seen in the very early development in the former of the mesoderm of the chorion and the very early differentiation of the connecting stalk and the structures related to it, viz. the primitive streak primordium, the cloacal membrane and the allanto-enteric diverticulum. Further, the presence of the ectoderm on the cranial surface of the umbilical stalk must be regarded as a preparation for the development of the umbilical cord.

The existence of the stalk offers a certain resistance in the development of the caudal parts of the embryonic body and complicates that development in the following respects: (1) The extension of the amniotic cavity towards the tissue of the stalk (in the caudal and dorsal direction) can be effected only by means of an activity of the stalk ectoderm by which the mesoderm of the stalk is partially destroyed. (2) The yolk-sac penetrates into the connecting stalk in the form of a narrow diverticulum which enlarges and eventually opens out again into the cavity of the yolk-sac. This process may probably be repeated several times. (3) The very early primordium of the allantois does not arise directly from the hind-gut (as in the lower Mammals) but from an allanto-enteric diverticulum. The orifice of this diverticulum later comes to form a part of the hind-gut. It is only in the stage when the insertion of the umbilical stalk has reached the ventral wall of the embryonic body that the allantois can be said to arise directly from the hind-gut, and so in this way the conditions characteristic of the lower Mammals are realised.

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DESCRIPTION OF PLATES I–III

Figs. 1–24. The figures are orientated so that the dorsal side is uppermost, unless otherwise stated. *Al.* allanto-enteric diverticulum; *Amn.* amniotic cavity; *Amn'.* diverticulum of the amniotic cavity below caudal end of embryo in the median plane; *Cl.* cloacal membrane; *Ect.* ectoderm; *Emb.* caudal end of the embryo; *Ent.* entoderm; *Ent'.* entoderm of the hind-gut; *Ent''.* entoderm close cranial to the orifice of the allanto-enteric diverticulum; *Ch.* chorion; *Ch.c.* chorionic cavity (extra-embryonal coelom); *Mes.* mesodermal mass lying free in the amniotic cavity.

Plate I

Fig. 1. Embryo Bi II, section 330. ×300. Cloacal membrane in its best developed part. Dorsal side on the right, ventral side on the left.

Fig. 2. Embryo Bi II, section 327. ×400. The limits of the cloacal membrane towards the mesoderm are becoming indistinct. The limits of the ectoderm towards the mesoderm are indistinct laterally to the cloacal membrane. Text on p. 465.

Fig. 3. Embryo Bi II, section 326. ×400. The process given off by the ectoderm towards the entoderm of the allanto-enteric diverticulum is very indistinctly marked off from the mesoderm. Text on p. 465.

Fig. 4. Embryo Bi II, section 325. ×400. The limits of the remnant of the cloacal membrane are very indistinct. Underneath + are distinct granules (sign of cell-dissolution). Text on p. 465.

Fig. 5. Embryo Bi II, section 321. ×400. The ectoderm is connected with the entoderm by a single spindle-shaped cell. In the place marked by an arrow the ectoderm is thickened in a knot. Text on p. 465.

Fig. 6. Embryo Bi II, section 315. ×400. The ectoderm gives off a cell-cord which nearly reaches the entoderm. Between its end and the entoderm there are numerous granules (possibly products of cell-dissolution); such are also visible in the ectoderm and entoderm. The dorsal side of this section on the right, the ventral on the left. Text on pp. 465, 466.

Fig. 7. Embryo Bi II, section 314. ×400. The allanto-enteric diverticulum has a form of a flattened canal. In the dorsal direction (to the right) it sends a short process towards the ectoderm, in which granules are to be seen. In the ventral wall of the allantois (on the left) the entodermal cells contain vacuoles in their basal part; the nuclei are situated towards the free surface of the cells. Text on pp. 466, 467.

Fig. 8. Embryo Bi II, section 320. ×520. The limit between the ectoderm and the mesoderm is very indistinct, especially in the thickened knot (*) close to the median plane. Below + there is an ectodermal cell connected with the mesoderm by a distinct, long process. Text on p. 469.

Plate II

Fig. 9. Embryo Bi XI, section 261. ×400. The allantois close beneath its orifice into the hind-gut. Entoderm of the allantois consists of vacuolated cells. Dorsal side on the right, ventral on the left. Text on p. 467.

Fig. 10. Embryo Bi XI, section 276. ×400. Allantois far caudal to its orifice into the hind-gut. Otherwise as in fig. 9.

Fig. 11. Embryo Bi II, section 336. ×166⅔. Text on p. 466.

Fig. 12. Embryo Bi II, section 338. ×366⅔. Text on p. 466.

Fig. 13. Embryo Bi II, section 326. ×166⅔. The penetration of the ectoderm into the mesoderm (especially distinct at +). Text on p. 470.

Fig. 14. Embryo Bi II, section 326. ×520. The detail of the place marked by + in fig. 13. Text on p. 470.

Fig. 15. Embryo Bi II, section 322. ×520. Numerous granules in the mesoderm underneath the ectoderm (close to the insertion of the amnion to the connecting stalk).

Fig. 16. Embryo Bi II, section 335. ×166⅔. Text on p. 470.

PLATE III

Fig. 17. Embryo Bi II, section 335. ×480. Detail from fig. 16 (the place between th rows in fig. 16). The ectoderm is apparently absent in some places.

Fig. 18. Embryo Bi XI, section 301. ×613½. The penetration of the stalk ectoderm to the mesoderm in the form of a thickened knot. Text on p. 471.

Fig. 19. Embryo Bi XI, section 295. ×613½. A place similar to that in fig. 18. Text on p. 471.

Fig. 20. Embryo Bi XI, section 304. ×52. View of the amniotic cavity (*Amn.*) with the caudal end of the embryo, the chorionic membrane (*Ch.*) and the connecting stalk (on the right). In an outpocketing of the amniotic cavity there is a sequestered mesodermic mass (*Mes.*).

Fig. 21. Embryo Bi XI, section 284. ×613½. Ectodermal cells penetrating into the mesoderm of the connecting stalk (+, ∗). Text on p. 471.

Fig. 22. Embryo Bi XI, section 300. ×613½. Flattened ectodermal cells penetrating into the mesoderm of the connecting stalk (for example at +). Some of them have been shed into the amniotic cavity (marked by an arrow).

Fig. 23. Embryo Bi XI, section 298. ×613½. The flattened cells of the stalk-ectoderm are connected with the mesodermal cells by means of cytodesmata (+, ∗). Text on p. 471.

Fig. 24. Embryo Bi XI, section 315. ×93⅓. The sequestered mesodermal mass (*Mes.*) in an outpocketing of the amniotic cavity. This figure is turned through 90° in comparison with fig. 20.

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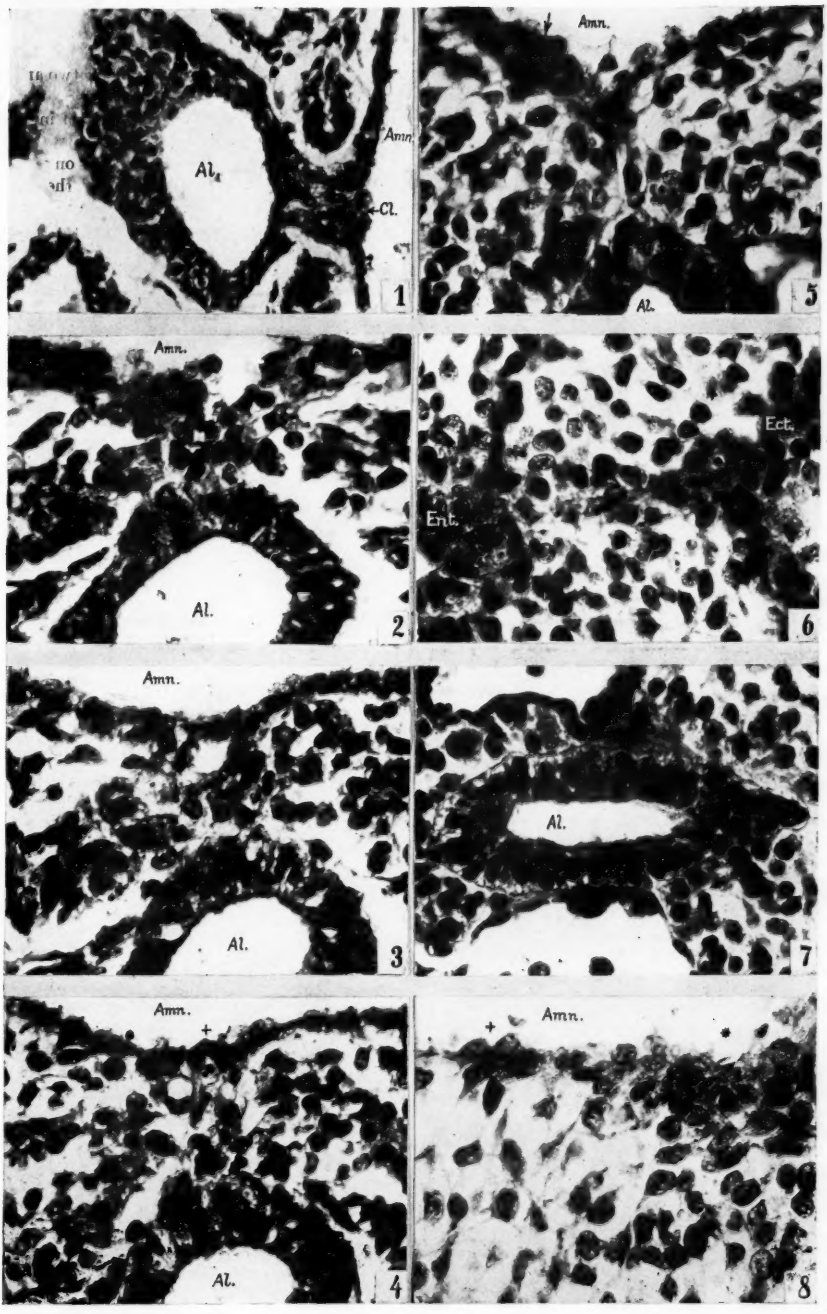

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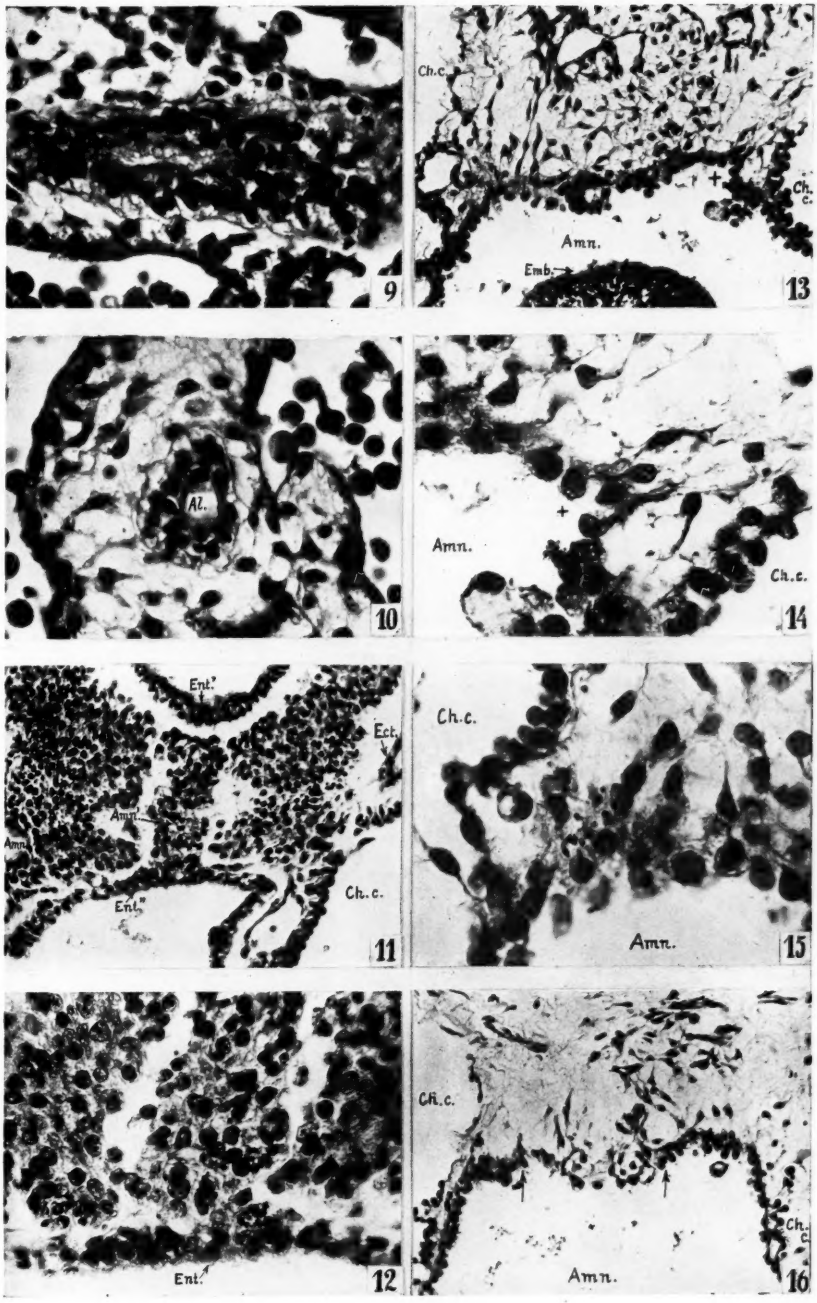

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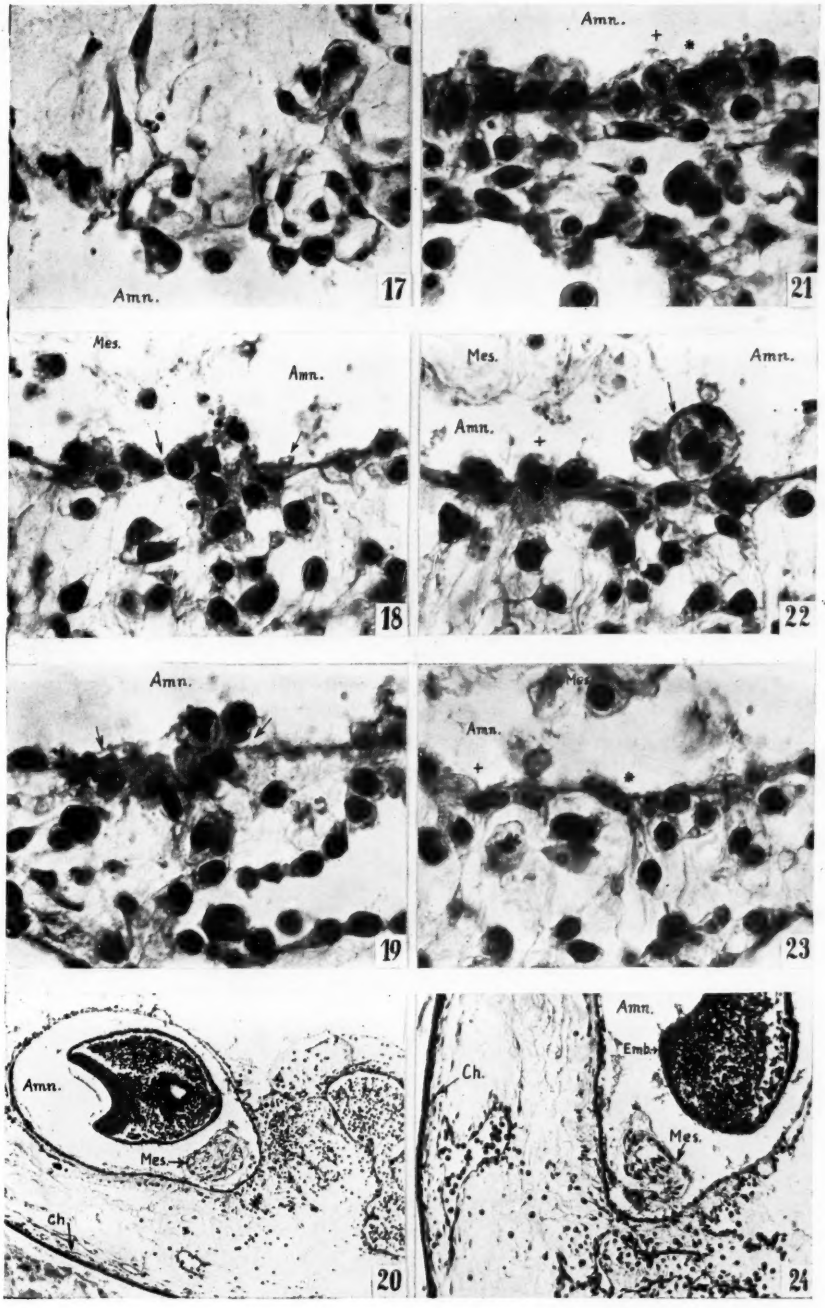
FLORIAN—The Formation of the Connecting Stalk and the Extension of the Amniotic Cavity towards the Tissue of the Connecting Stalk in Young Human Embryos



FLORIAN—The Formation of the Connecting Stalk and the Extension of the Amniotic Cavity towards the Tissue of the Connecting Stalk in Young Human Embryos

THE CORTICAL REPRESENTATION OF THE MACULA

By G. ELLIOT SMITH, F.R.S.

Professor of Anatomy, University of London

The development of the macula was responsible for adding to the optic nerves and tracts as many new fibres as the whole of the rest of the retina (peripheral) supplies. In the lateral geniculate body a new receptive nucleus of corresponding dimensions is provided to transmit macular impulses to the cerebral cortex. For many years neurologists have been speculating on the nature of the representation of the macula in the cerebral cortex. During the war Henschen's idea of "the cortical retina" was confirmed and corrected by the observations made upon wounded soldiers by Sir William Lister, Dr Gordon Holmes, and many other physicians.

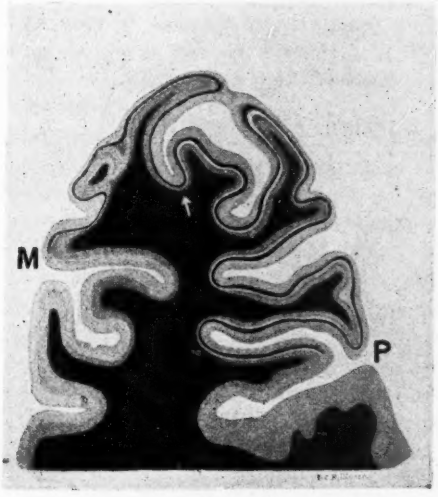


Fig. 1. Photograph (negative) of a horizontal section of the posterior part of a fresh cerebral hemisphere (human). *P*, medial part of the area striata representing the peripheral retina. *M*, lateral part representing the macula. The arrow points to the transition from the peripheral to the macular parts of the cortical retina.

Recently (1928) Prof. B. Brouwer and his collaborators, Drs van Heuven and Biemond, in Amsterdam have introduced a new precision into the cortical localisation of the macula in monkeys. Studying my own preparations of the human brain in the light of their truly epoch-making investigations, I was able

to detect with the naked eye a sudden change in the texture of the area striata at the place corresponding morphologically to that where in monkeys Prof. Brouwer and his colleagues located the boundary between the peripheral (*P*) and macular (*M*) territories.

In a horizontal section through the posterior pole of a human cerebral hemisphere the area striata, distinguished by the presence of the stria of Gennari, is seen to undergo a sudden change in character a short distance behind its midpoint. The thickness of the stria is reduced and the dark band (which is found on its inner side in the part representing the peripheral retina) disappears. The macular cortex begins at this place and extends around the pole on to the lateral surface of the hemisphere to end at the lip of the lunate sulcus. As this lateral part of the area striata is much broader than the medial part, exact measurements reveal the fact that the macular part is at least as extensive as the whole peripheral part. It is possible to identify the macular part of the area striata in many human brains by simple observation of the morphological features of the surface of the cerebral hemisphere. Looking at the posterior aspect of the hemisphere (see fig. 2, which represents the pole of the left hemisphere), three semilunar sulci—lunatus, polaris superior and polaris

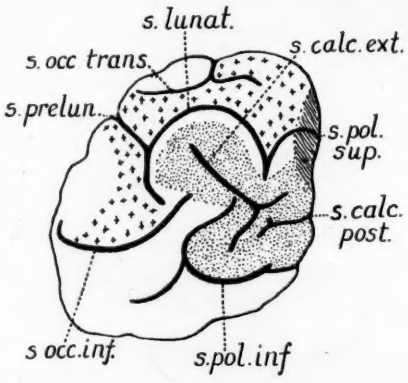


Fig. 2

inferior—may often be seen arranged in a trefoil or shamrock-leaf pattern (grouped around the calcarine sulci in the axis of the area striata). The rapid expansion of the lateral part of the area striata to afford cortical representation of the macula is responsible for the formation of three opercula bounded by these three semilunar sulci. Hence the presence of this cortical shamrock pattern affords definite evidence of the position and extent of the macular area.

OBSERVATIONS ON THE GROWTH OF THE SUPRARENAL CORTEX

By W. C. OSMAN HILL, M.D., Ch.B. (Birm.)
Department of Anatomy, University of Birmingham

The relatively enormous size of the human suprarenal gland at the time of birth has long been a matter for remark. The exact time at which the fact became known is not certain, but mention is made of it by J. F. Meckel in 1812 and by Johannes P. Müller in Hildebrandt's *Anatomie* (1830–2). In the French translation of Meckel's work are many interesting facts relating to the size of the suprarenals in Man. He quotes Bichât as stating that the suprarenal disappears entirely in old age; and he remarks that he himself has discovered enlarged suprarenals in those whom he has known to have been "addicted to the pleasures of love." The foetal hypertrophy of the gland was evidently recognised even earlier than this, since Meckel (14) himself quotes G. B. Morgagni (1682–1781) as having discovered the suprarenals to be of small size in the anencephalic foetus, which indicates that the normal foetus was well known to have a large suprarenal.

The earliest detailed study of the development of the suprarenal was the work of M. Gottschau who published a number of papers on the suprarenals of Man and the rabbit (6) (1883). No reference is made in Gottschau's writings to the zoning of the cortex. A closer investigation into the facts relating to the relative size of the suprarenals in the anencephalic and in other abnormal foetuses was made by R. Magnus (13) (1889). He found no case of anencephaly with a normally sized suprarenal, though he gives reference to cases where one large and one small gland had been found. He noted that the gland was normal in hydrocephaly.

The next step was the publication of R. Zander's classical paper (20) on the suprarenals (1890). After alluding to Meckel's remarks, he proceeded to give the weight of the suprarenals at various ages in Man relative to the weight of the kidney. He noted the fact that in other mammals (calf, sheep, cat and hedgehog) the gland is not so large in comparison with the kidney as in Man. Apart from the fleeting statement made by Meckel quoted above, Zander seems to have been the first to point out the close connection existing between the suprarenals and the sexual apparatus. He particularly noted that the suprarenals were larger in the Negro, thus correlating them with the larger sexual organs in that race. He made a further comparison by recording the weight of the suprarenals and the gonads in various foetal monsters. A reference was made to a case of anencephaly possessing normal suprarenals recorded by Klein.

The comparative anatomy of the suprarenals was very extensively studied by A. Pettit (15) (1896). No details were given of the evolution of the different parts of the cortex of the gland in the animals studied. This was, however, done later (1906) by H. Poll in Hertwig's *Handbuch* (16). In this account are to be found good figures of the appearances of the cortex in the foetal sheep and foetal pig. No mention is made here, however, of any transitory part of the cortex. About the same time appeared the study by T. R. Elliot and I. Tuckett (4) on the suprarenal of the guinea-pig. They noted the small size of the gland at the time of birth, and the appearance of a relatively huge cortex during adolescence. In *Cavia* and *Coelogenys*, according to these authors, the cortex is larger in proportion to the rest of the gland than in any other mammal.

The actual reason for the large size of the human gland at birth was discovered almost simultaneously by S. Starkel and L. Wegrzynowsky (18) (1910), by T. R. Elliot and R. G. Armour (3) (1911), by H. Kern (10) (1911) and by Erwin Thomas (19) (1911). All these workers mention the presence of a special zone of cortex lying between the true or adult cortex and the medulla. This has since come to be known as the "boundary zone" or "foetal cortex." By Starkel and Wegrzynowsky it was referred to as "Markzone." These authors drew attention to important vascular changes occurring in this layer of cortex after birth, whilst Elliot and Armour showed that the newly found zone underwent a process of involution after birth. The last-named writers also showed that the small size of the suprarenal of the anencephalus is due to an almost complete absence of the zone of cortex in question. Another important statement made by Elliot and Armour is that this "foetal cortex" is a structure peculiar to the human subject, not having been found by them in any other mammal. The only evidence for this seems to be a reference to the earlier paper by Elliot and Tuckett (4) on the suprarenal of the guinea-pig. They admit that apes were not examined. In Kern's contribution (10) there is an accurate description of the process of involution of the "foetal cortex" after birth in Man and a mention of the vascular changes associated with this process. He also examined several other animals to ascertain if a similar process could be found among them and came to the conclusion that no such analogous condition was present. This seems not unreasonable when one reviews the age of some of the animals examined by him. These included guinea-pigs (2–3 weeks), rabbits (2–5 weeks), calf (4 weeks), ox (4 years), pig (6 months), sheep (6 months), rat (6 weeks) and horse (16 years). In the paper by Thomas attention is drawn for the first time to the naked-eye appearances observable in the gland during the process of involution of the foetal cortex in Man. He especially noted the pale peripheral zone corresponding to the true cortex and the darker blood-containing zone lying deep thereto.

E. E. Glynn (5) in 1912 published results of his work on the times at which the various changes occur in the evolution of the adult type of suprarenal cortex in Man. He pointed out that the three zones of the adult cortex are all

recognisably present by the end of the second post-natal month. He also drew evidence to show an important connection between the cortex and the sexual apparatus. W. Dewitzsky (1) (1912) studied the histology of the gland in rats and other animals chiefly in reference to the growth of the medulla. He made references to the work of Kern and Thomas, but failed to find the "foetal cortex" in the animals he examined.

C. M. Jackson (8) (1913) made a study of the post-natal growth of various organs including the suprarenal in the albino rat. This was followed by a more detailed analysis of the suprarenal of the rat by the same author (9) (1919). He came to the following important results: (i) in normal post-natal development both cortex and medulla of the gland increase during the first year; after which the two structures grow at different rates; (ii) all three histologic cortical zones are present at birth; (iii) there is no definite cortico-medullary boundary in the earlier stages on account of the fact that islands of cortical tissue are found embedded in the medulla. These are absorbed later, thus giving the characteristic cortico-medullary boundary of the adult gland. Some of the islands remain isolated in the medulla for a considerable time after birth. The date of the occurrence of these changes is variable. Jackson made references to the previous work of Gottschau, Pfaundler and Soulié who had mentioned atrophic changes occurring in the deeper cortical zone in the rat and other animals. He came to the general conclusion that probably a zone of atrophic cortical tissue would be found in the young animal in the deeper parts of the cortex of the suprarenal and that it was probably due to the absorption of this tissue that the definite cortico-medullary boundary was produced.

Meanwhile in the same year J. C. Donaldson (2) had come to the opposite view. This writer had studied the relative volumes of cortex and medulla in the suprarenal of the rat. He discovered no degenerative phase in the growth of the suprarenal comparable with that occurring in the human gland.

The next step in the development of our knowledge of the cortex of the suprarenal was made by studying the lipoid content of the gland. Elliot and Armour (3) in their original description of the foetal cortex had been able to identify this structure chiefly on account of a conspicuous absence of fatty bodies, thus causing a contrast with the fasciculate zone of the true cortex with its cells heavily laden with lipoids.

M. F. Lucas Keene and E. E. Hewer (11) (1924) examined the lipoid content of all parts of the human gland at different stages of foetal life. They were able to show that the foetal cortex as well as the true cortex is capable of showing a reaction with Sudan III, though it does so happen that at the time of birth the foetal cortical zone is deficient in fatty substances. Nevertheless at earlier stages they were able to show lipoid present in the foetal as well as in the true cortex, the staining being "very intense" by the 32nd week. They obtained this reaction also with anencephalic suprarenals. Moreover, it had been stated by Schafer (17) (1924) that the disappearance of the foetal cortex after birth was due to a fatty degeneration of its cells and therefore a reaction with Sudan III

would be expected at this stage also. In a later paper (12) by Lucas Keene and Hewer (1927) the development of the human gland was reviewed in more detail, and a suggestion made that the problems connected therewith would probably find elucidation only on a study of the comparative development of the gland. In the same paper it is again stressed that lipoid can be seen in the foetal cortex by the 24th week and that this increases in amount more rapidly in the true than in the foetal cortex. They point out that the degeneration of the foetal cortex is associated with a diminution in the lipoid content.

Lastly E. Howard-Miller (1927) published results of a study of the suprarenal cortex of the young mouse. In this paper (7) a new zone of cortex having age and sex relationships is described as the X-zone, and a comparison is made with the foetal cortical zone of Man. The X-zone is a transitory zone situated at the cortico-medullary boundary. It is present in both sexes at birth, but disappears early in the male. In the female it is still growing at four weeks, and its degeneration is associated with the animal's first pregnancy. The degeneration is said to be similar to that involving the human foetal cortex, but not to be at an analogous age period. Degeneration is associated with vacuolation of the cells and hyperaemic changes.

Summing up it may be said that the main trend of the more recent work on the foetal cortex points to the fact that some similar change might well be looked for among other mammals, in spite of the earlier findings of Elliot and Armour, Kern and Thomas and the isolated remarks of Donaldson. Accordingly in the present investigation the cortical structure of the suprarenal gland has been studied in the late foetal and early post-natal stages of a number of mammals. As all previous observations have been mainly confined to rodents, this order of mammals has not been investigated. Attention has therefore been directed to the lower Primates, the Carnivores and the Ungulates.

MATERIAL AND METHODS

The suprarenal glands of a number of lower Primates, Carnivores and Ungulates have been studied by means of dissections, sections and microscopical preparations.

With regard to shape and relations, the glands have been compared with that of Man, and the human gland at birth has been taken as a general standard of comparison in reference to size; but in most cases the gland has been compared in size with the kidney also. Measurements of the gland in its cranio-caudal, side to side and antero-posterior directions have been recorded.

Sections have been taken in the sagittal and coronal planes and examined by the naked eye. For this purpose absolutely fresh material is of course essential. Under these circumstances it is generally possible to identify the chief zones, and in the case of sagittal sections, to see the way these are disposed around the central vein. Many important colour changes can also be recognised by this method.

For histological purposes the material was fixed in equal parts of Müller's fluid and Bouin's aqueous picro-formol-acetic acid, or in equal parts Müller and 4 per cent. formalin. It is maintained that the cells of the cortex should be recognisable by their morphological characters alone; although it must be remembered that it was chiefly on account of the absence of lipoid in the cells of the foetal cortex that Elliot and Armour made their discovery of the presence of this zone in the human gland at birth. Later work, however, showed that the mere absence of lipoid is not sufficient to diagnose foetal cortex, since at certain stages this substance is present in the foetal as well as in the true cortex.

Accordingly the opinion is expressed that foetal cortical cells should be distinguished from true cortical cells by their larger size, swollen appearance, tendency to degeneration, vacuolated nuclei, and especially by their environmental vascular changes—engorgement of radial vessels and haemorrhage.

Therefore, although some sections have, for comparison with the human gland, been stained with Sudan III to show the presence of lipoid, most of the microscopic work has been done with sections stained with Mayer's haemalum and counterstained with eosin. It is with eosin that the cells of the foetal cortex show their most characteristic reaction.

I. PRIMATES

The suprarenal glands of the following Primates have been examined:

(i) Adult macaques of various species.
(ii) Foetal macaques at full term.
(iii) Adult marmoset.
(iv) Foetal lemur at full term.
(v) Foetal *Nycticebus* at half term.

Some idea of the relative sizes of the suprarenals of a series of Primates is given in fig. 1.

Adult Macaques

The following measurements are of the suprarenal gland of a number of adult macaques:

Macacus cynomolgus, female, left	17 mm. by 14 mm.
Macacus cynomolgus, female, right	17 mm. by 10 mm.
Macacus rhesus, male, left ...	15 mm. by 9 mm.
Macacus nemestrinus, male, right	15 mm. by 13 mm.

In adults of this genus it is seen that the suprarenal gland is variable in size relative to the kidney; the variations being in relation to species, sex and age (cf. Schafer (17)). The gland is larger in the female than in the male, and section of the gland even to the naked eye proves that this increased size is due to cortex rather than to medulla. In the male the gland is small, flattened antero-posteriorly and its cortical rim is thin and pale. In a recently pregnant

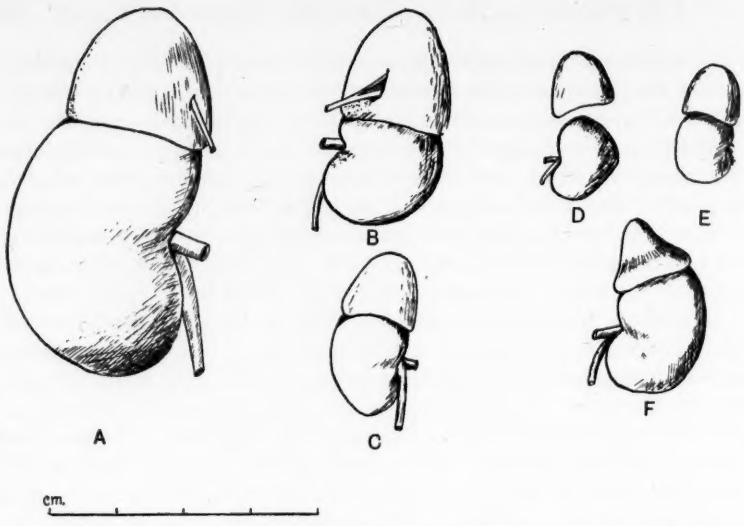


Fig. 1. Kidneys and suprarenals of a number of adult and foetal Primates all drawn to the same scale. A. Right kidney and suprarenal of adult male *Macacus nemestrinus*. B. Left kidney and suprarenal of foetal male *Macacus* hybrid. C. Left kidney and suprarenal of foetal male *M. pileatus*. D. Right kidney and suprarenal of foetal male *Lemur niger*. E. Left kidney and suprarenal of foetal male *Nycticebus tardigradus*. F. Left kidney and suprarenal of adult male *Hapale jacchus*.

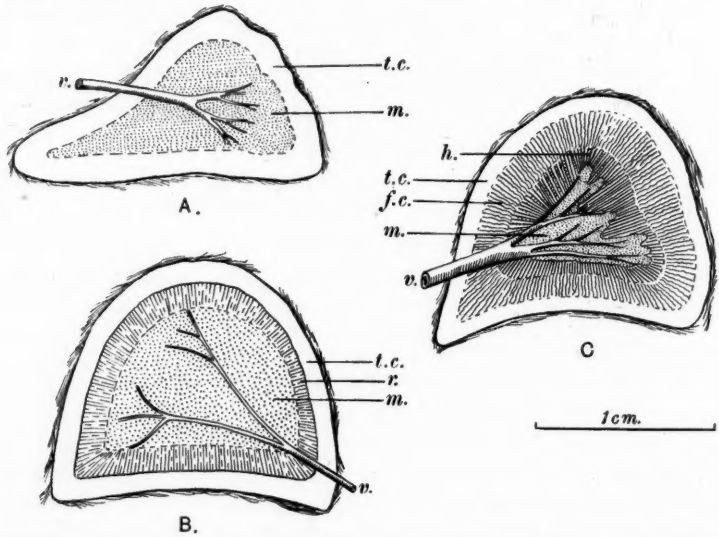


Fig. 2. Coronal sections of the suprarenals of different Primates to show naked-eye appearances of the gland. All drawn to the same scale. A. Suprarenal of adult male *Macacus rhesus*. B. Suprarenal of adult female *M. cynomolgus*. C. Suprarenal of foetal male *M.* hybrid. *t.c.* true cortex; *r.* reticular zone; *f.c.* foetal cortex; *h.* haemorrhagic zone of foetal cortex; *m.* medulla; *v.* central vein.

female the cortical rim was thick and more vascular than in the male. Microscopic sections showed the depth of the cortex in the female to be due to a thick layer of deep cortex corresponding to the human zona reticularis. In an older male *M. rhesus* the zona reticularis was found to be completely absent. This seems to have some bearing on the phenomena associated with the "X-zone" described in the suprarenal of the mouse by Howard-Miller (7).

Foetal Macaques

The size of the suprarenal gland in the full-term foetal macaque can be judged from fig. 1, B and C. The drawings were taken from a new-born male *M. cynomolgus* × *M. pileatus*, and a nearly full-term foetal *M. pileatus*. The gland is in each case almost as large as the kidney itself, so that in this respect it closely approaches in its relative size the human gland at the same stage of development. Measurements of the suprarenals of the above foetal macaques are as follows:

M. cynomolgus × *M. pileatus* (male) hybrid

Left suprarenal

Height	17·5 mm.
Breadth	15·0

M. pileatus (male)

	Left suprarenal	Left kidney
Height	10·0 mm.	16·0 mm.
Breadth	10·5	10·5
Thickness	6·5	8·5
	Right suprarenal	**Right kidney**
Height	9·0 mm.	16·0 mm.
Breadth	12·0	11·0
Thickness	6·5	9·0

On section the suprarenal of foetal macaques presents to the naked eye the same appearances as the human foetal suprarenal (see fig. 2). Thus beneath the fibrous tissue sheath of the gland there is first a thin rim of pale yellowish or cream coloured cortex of firm consistence. This is succeeded by a thick zone of darker friable tissue which at first sight might be taken for medulla. The deepest parts of this friable zone may be darker than the rest on account of a greater vascularity or even from the presence of actual haemorrhage. In the middle of the gland the central vein is seen in section.

Microscopically the most striking fact is that the gland consists almost entirely of cortex as in the case of the human foetal suprarenal (see figs. 3 and 4). Medullary tissue is represented only by a few clumps of chromaffin cells around the central blood vessel and amongst the deepest cells of the cortex.

The cortex of the suprarenal on the other hand shows a well-marked differentiation into two zones. The differentiation is clearly visible in sections stained both by the Sudan III method and by the haemalum and eosin method. The outermost part of the cortex consists of small cells with darkly haematoxylin-staining nuclei. These cells are more closely aggregated just beneath

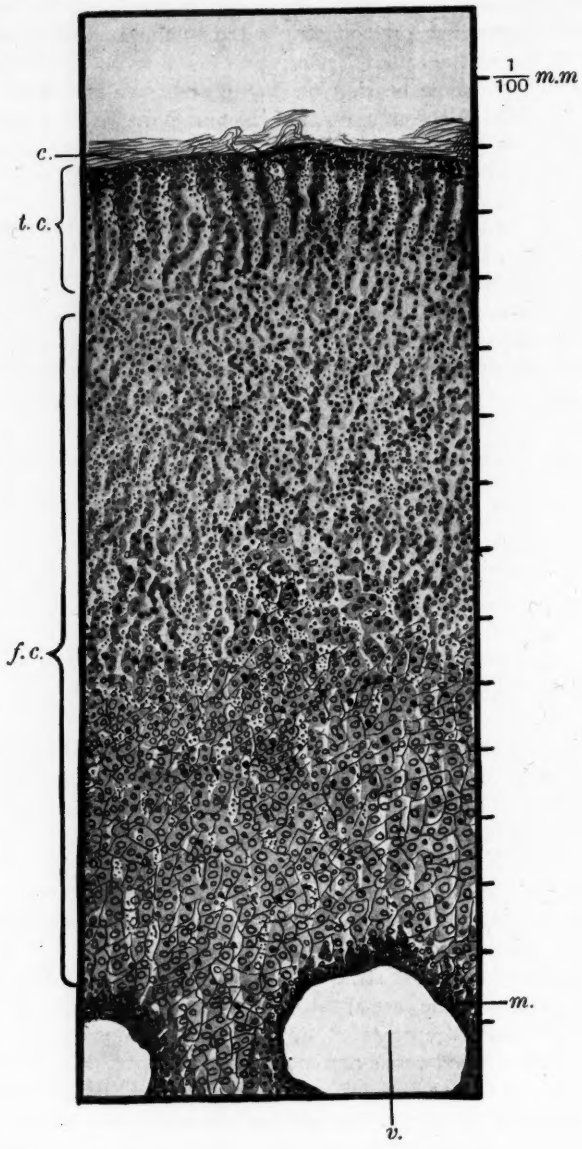


Fig. 3. Microscopic appearances of the suprarenal of foetal *M. pileatus*. *c.* capsule; *t.c.* true cortex; *f.c.* foetal cortex; *m.* medulla; *v.* central vein.

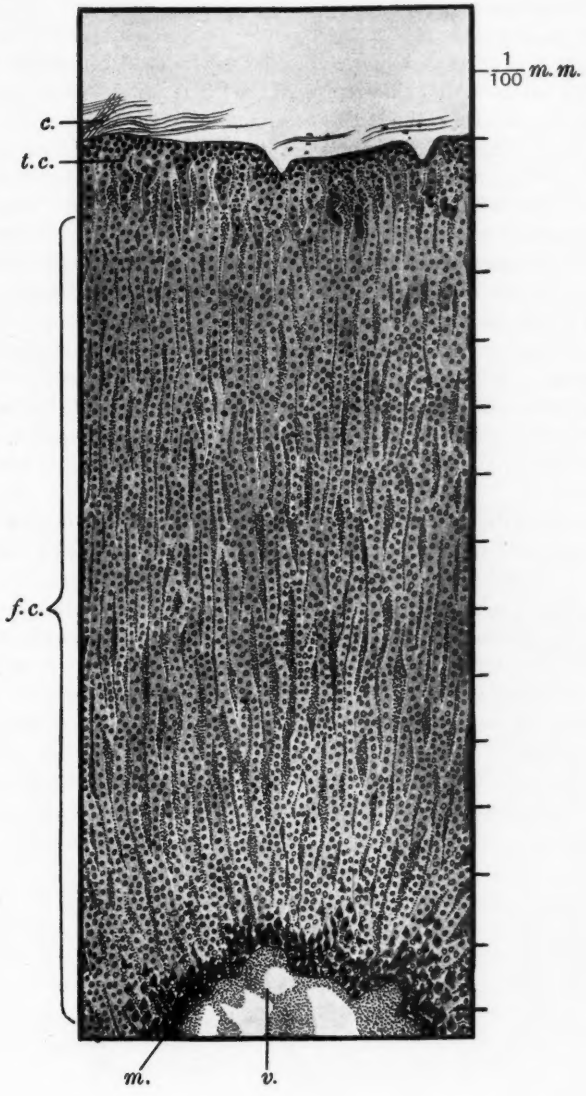


Fig. 4. Microscopic appearances of the suprarenal of an older foetal *M.* hybrid showing vascular changes.
c. capsule; *t.c.* true cortex; *f.c.* foetal cortex; *m.* medulla; *v.* central vein.

the capsule, but it cannot be said that they form a definite glomerular arrangement. The deeper layers of these small cells form columns descending into the depths of the gland substance even in the younger specimen. In sections of the suprarenal of the younger of the two specimens examined none of the cells of the outer part of the cortex show any lipoid reaction with Sudan III. There can be no doubt, however, that they represent the "true cortex" of the adult gland. The rest of the gland, i.e. the part corresponding to the friable zone described above, consists of totally different cells. These are large, pale and have large degenerate-looking nuclei. The boundary between this zone and the suprajacent one is not definite, for the cells of the "true cortex" are seen to be insinuating themselves between the uppermost strata of the zone under consideration. The more superficial cells look more degenerate than the deeper ones. They are pale and vacuolated and stain poorly. In sections stained by Sudan III the deepest cells of all are heavily loaded with lipoid. This proves conclusively that presence of lipoid cannot be used as a diagnostic sign ruling out the presence of "foetal cortex," since there can be no possible doubt that these large pale cells represent that structure (*a*) because of the comparative size of the gland, (*b*) because practically the whole gland consists of cortex, and (*c*) because of the obvious differentiation of the cortex into two morphological zones.

In sections of the suprarenal of the older of the two foetal macaques stained by haemalum and eosin a further stage in development is seen (fig. 4). This consists of a massive engorgement of the radial blood vessels which spread outwards from the central vein into the cortical substance. In the specimen under consideration the vessels of the deeper half of the foetal cortex have undergone this engorgement. More superficially the vessels contain large masses of blood corpuscles, but not so many as those deeper in. Here and there appear one or two small areas of haemorrhage, where the engorgement has been so extreme as to cause actual rupture of the vessel wall. As would be expected the cells of the foetal cortex in this older specimen show a greater degree of degeneration than in the younger example.

Adult marmoset (*Hapale*)

In an adult male of this genus the suprarenal was found to be larger in comparison with the kidney than in Man (fig. 1). The gland has a conical shape, being almost as thick at the base from before backwards as from side to side. The measurements are as follows:

	Left suprarenal	Left kidney
Height	7 mm.	16 mm.
Breadth at base	8	12
Thickness at base	5	8

The surface of the gland is wrinkled as in all adult Primates, suggesting removal of some deep tissue at an earlier stage. It is triangular in sagittal section. Microscopically it is made up of a central nodule of medulla which

accounts for about one-third of the organ. Extensions of medulla into the cortex take place in the angles of the triangle. The cortex consists throughout of well-formed cells of which the outer third are small and show no lipoid reaction, whilst the remainder are arranged in columns radiating outwards from the medulla and which show a heavy lipoid reaction. There is no zona reticulata (cf. adult male *Macacus*).

Lemuroids

The suprarenals have been examined in a *Lemur niger* at full term, and in a *Nycticebus tardigradus* at about mid term. The relative sizes of the glands and the kidneys can be judged and compared with those of other adult and foetal Primates from fig. 1. Measurements are as follows:

Lemur niger, full term, male

	Left suprarenal	Left kidney
Height ...	9 mm.	11 mm.
Breadth	7	7
Thickness	2	3

Nycticebus tardigradus, half term, male

	Left suprarenal	Left kidney
Height ...	5·5 mm.	7 mm.
Breadth	5·5	4
Thickness	3·5	5

In each case therefore the suprarenal gland at the stage examined is shown to be almost as large as the kidney, and thus to agree with the human foetal gland.

In both cases section reveals the gland to consist, as in *Macacus* and Man, almost entirely of cortex. This cortex, moreover, is, even in the mid-term stage of *Nycticebus*, well differentiated into two very obvious zones; a peripheral zone of true cortex and a deep zone of "foetal cortex."

In *Nycticebus* the true cortex consists of a very thin margin of tiny cells with very darkly staining nuclei. There is as yet no evidence of invasion of the "foetal" zone. The foetal cortex consists of large rounded cells arranged in columns radiating from the centre of the gland. Between the columns there is loose reticular tissue containing vessels. The vessels, however, are not engorged. The reticular tissue is more plentiful near the middle of the gland.

In both forms of Lemuroids examined the medulla is very sparse. On section no boundary can be seen between cortex and medulla since practically the whole gland consists of cortex.

II. CARNIVORA

The suprarenals of the following Carnivores have been examined:

(i) New-born kittens of both sexes.
(ii) New-born leopard cub.
(iii) New-born pups.
(iv) Pup, 4 days old.
(v) Young pups, 11 and 13 days old.
(vi) New-born bear cub.

In none of the above, with the exception of the leopard cub, does the suprarenal at or about the time of birth exhibit such marked enlargement in comparison with the size of the kidney as in Primates (see fig. 5). In the leopard cub the gland was certainly relatively larger than in new-born kittens as is shown in fig. 5. On the contrary in the bear cub the gland was comparatively minute. It is therefore useless to draw conclusions from the size of the gland only. Moreover in the dog, in which the changes in the gland have been followed in most detail, there is no very obvious diminution in the relative size of the suprarenal during the time immediately after birth comparable with that seen in Primates. There is consequently no shrivelling of the surface of the gland; the adult gland having as smooth a surface as that of the full-term foetus.

The following are measurements in millimetres of the suprarenals and kidneys in a number of Carnivores:

	Suprarenal			Kidney		
	Height	Breadth	Thickness	Height	Breadth	Thickness
Kitten, full-term male (left)	3·5	6	2·0	18·0	14·5	9·5
Kitten, full-term female (left)	4·0	8	2·5	15·0	13·0	5·5
Leopard cub, male (left)	12·0	9	7·0	22·0	19·0	12·0
Pup, full-term male (right)	4·0	7	2·5	18·0	10·0	8·0
Pup, 4 days old female (right)	3·5	7	2·0	20·0	13·0	9·0
Pup, 11 days old female (left)	5·0	10	—	30·0	20·25	15·0
Bear cub, male (right)	4·0	5	2·0	16·5	10·0	1·25

On section the suprarenal of any of the Carnivores examined shows to the naked eye that both medulla and cortex are present at the time of birth. Medulla, however, is less well developed than cortex. Microscopically the boundary between the cortex and medulla is not a definite line as in the adult gland. There are islets of cortex scattered irregularly in the substance of the medulla and masses of cortex projecting downwards from the main cortical layer into the medulla. As the animal grows older this arrangement is lost and a definite boundary comes to be formed between medulla and cortex. This

arrangement is shown in the section taken from the suprarenal of an 11-day-old pup in fig. 6 and compared with a section of the gland of an adult dog.

With regard to the details of cortical structure the following facts have been ascertained. Beneath a relatively thick capsule in the new-born pup's suprarenal there is a well-formed zona glomerulosa of much greater relative dimensions than that seen in the suprarenal of any of the Primates. This zone consists of flask-shaped masses of tall columnar cells arranged side by side in a single layer. They show a definite lipoid reaction. The rest of the cortex consists of

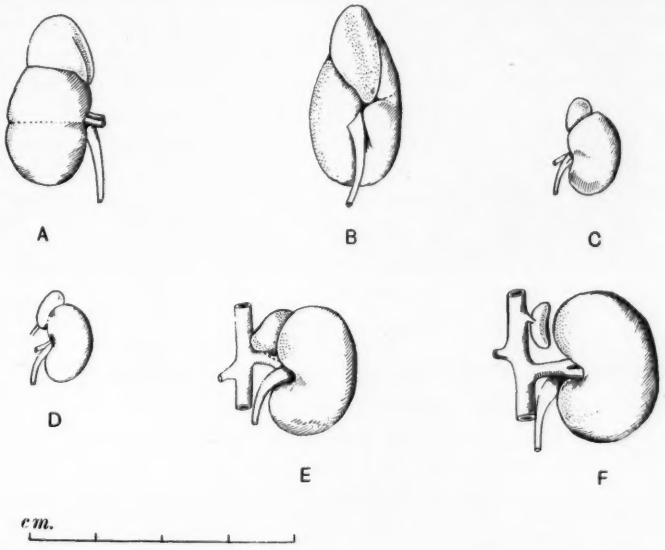


Fig. 5. Kidneys and suprarenals of a number of Carnivores. All natural size. A. Leopard cub, new-born male. Right kidney and suprarenal from in front. B. The same. Left kidney and suprarenal from the medial aspect to show the extent of the descent of the suprarenal over the upper pole of the kidney. C. Bear cub. Right kidney and suprarenal from behind. D. Kitten, new-born female. Left suprarenal and kidney from the front. E. Pup, new-born male. Right kidney and suprarenal from behind. F. Pup, 11 days old female. Left kidney and suprarenal from the front.

large ovoid cells arranged roughly in short columns radiating from the centre of the gland. Neighbouring columns intercommunicate and give a general reticular appearance (see fig. 6). These cells also show a lipoid reaction, the reaction being more intense as one approaches the medulla.

It is difficult to state what part of the suprarenal of young Primates corresponds to this deep zone of cells in the suprarenals of young Carnivores. The large size and general arrangement of the cells seems to point to their equivalence to the main mass of cortex of the young Primate suprarenal, i.e. to the so-called "foetal" cortex. It must be pointed out, however, that this layer of

cortex does not entirely disappear in the Carnivores as it does in Primates, but persists deep to the glomerular zone as the zona fasciculata, though it is a moot point, according to the present investigation, whether the zona fasciculata of Primates, with its small cells growing in from the zona glomerulosa, is comparable with the zona fasciculata of Carnivores with its large cells present from the first and independent of the glomerular zone, which is in itself a more bulky stratum than in Primates.

It must be pointed out that the suprarenal of the adult dog differs from that of the pup in having a decided boundary between cortex and medulla. The medulla has grown of course in quantity and contains no islands of cortex. The cortex consists of a well-developed zona glomerulosa of even greater proportions than in the pup; succeeded by a zone of reticular arrangement of comparatively less depth than in the pup. It would appear that some absorption of cortical tissue at the cortico-medullary boundary occurs in the period immediately following birth as Jackson (9) suggested might be found. This absorption however is never so massive as is seen in Primates and never involves as much of the cortical tissues. Cortical tissue corresponding to the so-called "foetal" cortex would appear to persist as the deep layer of the adult cortex.

III. UNGULATA

The suprarenals of the following Ungulates have been examined:

(i) Lamb at birth (female).
(ii) Lamb, 2 days old (male).
(iii) Lamb, 5 weeks old (male).
(iv) Adult sheep.
(v) Pig at birth (both sexes).
(vi) Pig, 24 hours old (both sexes).
(vii) Pig, 5 days old (both sexes).
(viii) Pig, 6 days old (male).
(ix) Adult pigs.
(x) Foetal hippopotami.
(xi) New-born goat.
(xii) Foetal calves.

In all cases the suprarenal at the time of birth does not show any marked enlargement when compared with the adult gland in the same species (see fig. 7).

Measurements of various foetal glands are shown in the accompanying table, in millimetres.

The adult gland is always comparatively well developed when contrasted with the gland of adult Primates. It never shows a wrinkled surface, so that, as in Carnivores, it can be assumed that there is never any gross removal of deep tissue during the evolution of the adult type of gland from the foetal

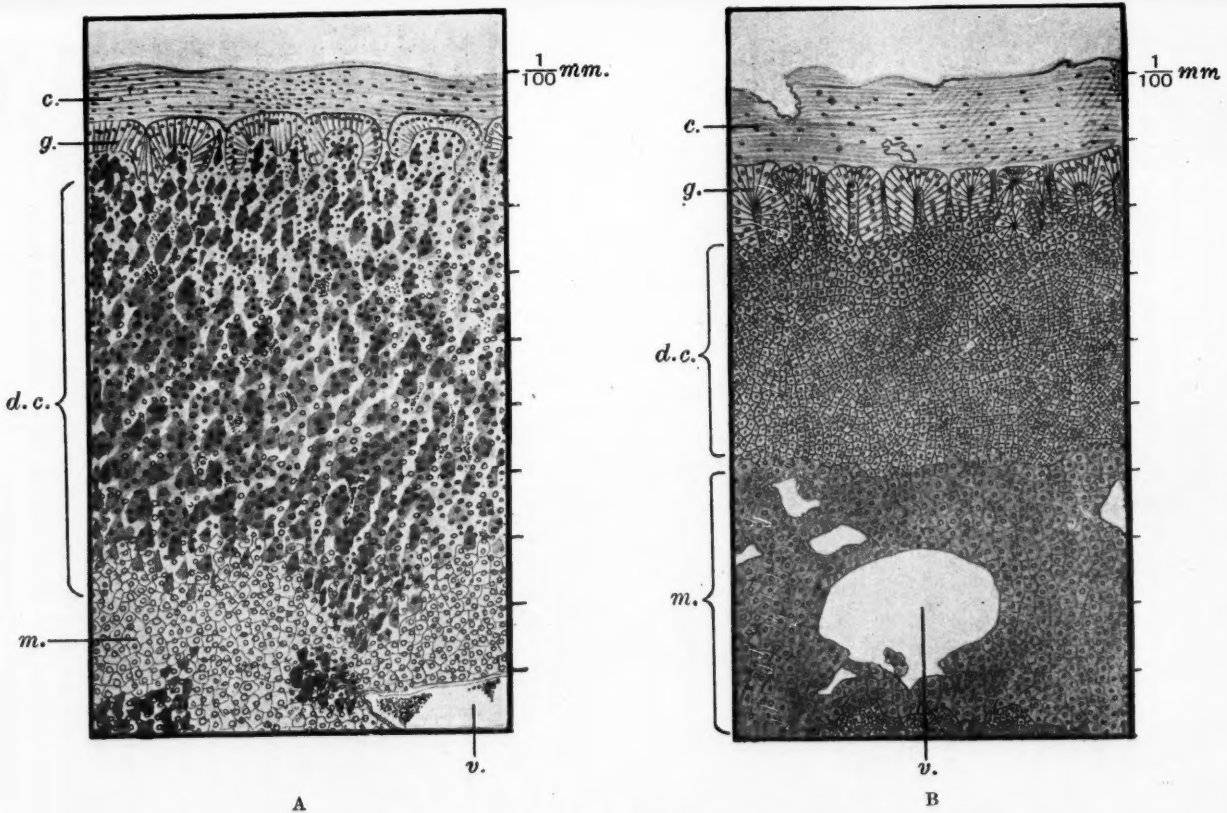


Fig. 6. Microscopic appearances of the suprarenal of: A. Pup, 13 days old; B. Adult dog.
c. capsule; *g.* glomerular zone; *d.c.* deep cortical zone; *m.* medulla; *v.* central vein.

organ. In most of the Ungulates examined the suprarenal is an elongated structure lying with its long axis transversely to the long axis of the kidney, but with one of its poles curving downwards and inwards towards the hilum of the corresponding kidney. The goat is an exception to this, for in this animal the suprarenal is a rounded organ, and in a new-born kid was about the size of a pea. In adult animals the suprarenal does not reach as far as the hilum of the kidney as it does in new-born animals, so that the gland becomes relatively shorter with age.

	Suprarenal			Kidney		
	Height	Breadth	Thickness	Height	Breadth	Thickness
Pig, 24 hours old female (left)	5·5	15·0	4·5	44·5	20·0	16·0
Pig, 24 hours old male (right)	—	—	—	29·0	13·25	10·5
Pig, 5 days old female (right)	5·0	13·0	6·5	35·25	16·0	13·5
Pig, 5 days old male (right)	5·0	14·5	5·5	33·0	17·0	11·5
Pig, 6 days old male (right)	4·0	17·0	5·5	37·0	18·5	6·0
Hippopotamus, foetal male	4·0	15·0	6·5	36·0	19·0	13·5
Lamb, 2 days old male (right)	7·0	17·5	6·0	34·0	26·0	16·0
Goat, 24 hours old male (right)	6·5	6·0	4·0	23·0	19·0	12·0
Calf, mid-term male (left)	8·5	11·0	—	42·0	25·0	—

Sections of the suprarenal reveal to the naked eye the presence of cortex and medulla in all Ungulates at birth. In the adult there is a marked variation in the proportions of the cortex in different species. Thus in the sheep there is a very deep layer of cortex and but a small quantity of medulla, whereas in the adult pig there is a large amount of medulla and a thinnish rim of cortex around it. This difference is not so obvious in young suprarenals. Thus in new-born pigs there is little medulla and a deep cortical zone. The same is true of lambs and goats. In the pig the medulla comes to the surface at the hilum of the gland (see fig. 8). Little can be made out of the details of cortical structure in naked-eye sections of the gland, except that certain vascular changes are recognisable by the colour of the cut surface. There is a tendency in the young suprarenals of all the Ungulates examined at the time immediately after birth to show these vascular phenomena. They consist in engorgement of the cortex, with blood spreading out from the central vein along the radial vessels between the columns of cortical cells. In parts this engorgement is so great as to lead to rupture of the vessels with consequent extravasation of blood.

This is suggestive of the processes occurring in the Primate suprarenal at a corresponding age. To the naked eye these changes appear first as a distinct radial striation of the deeper parts of the cortex merging later into a general diffuse reddening of the whole cortex. These appearances were especially noted in the suprarenals of young lambs.

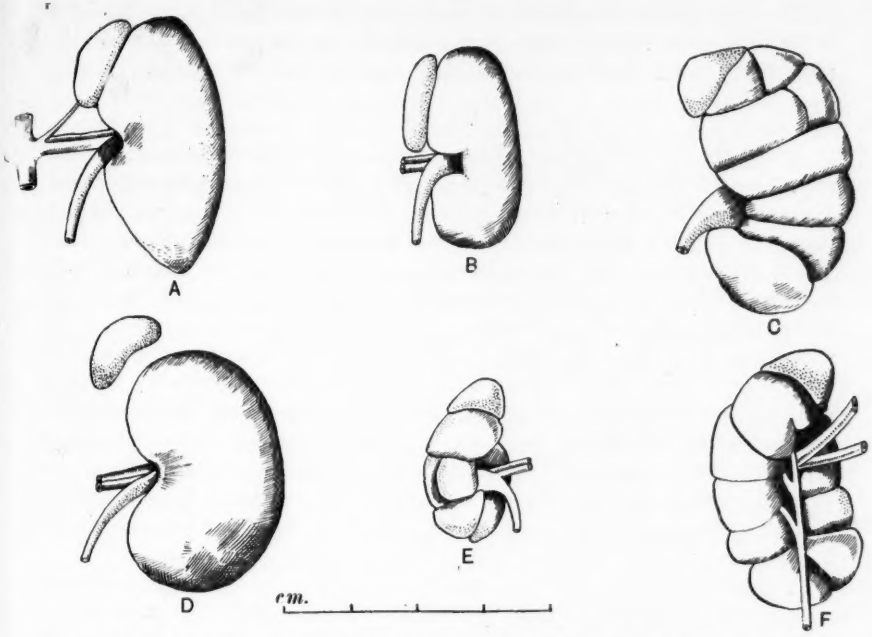


Fig. 7. Kidneys and suprarenals of a number of Ungulates. All drawn to the same scale. A. Pig, 24-hours-old male. Right kidney and suprarenal from behind. B. Pig, 6-days-old male. Right kidney and suprarenal from behind. C. Hippopotamus. Foetal male (mid-term). Left kidney and suprarenal from the front. D. Lamb, 2-days-old male. Right kidney and suprarenal from behind. E. Calf. Early foetus male. Left kidney and suprarenal from behind. F. Calf. Mid-term foetus male. Left kidney and suprarenal from behind.

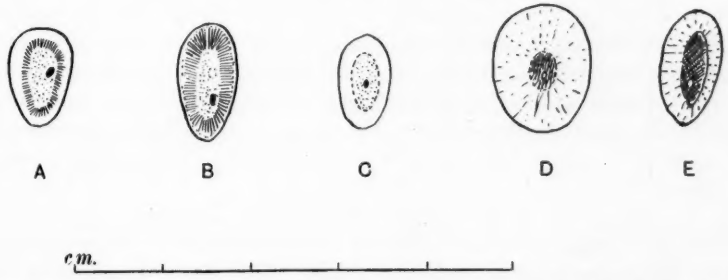


Fig. 8. Drawings of the naked-eye appearances of transverse sections of the suprarenals of a series of Ungulates. All drawn to the same scale. A. Lamb, 24 hours old. B. Lamb, 2 days old. C. Lamb, 5 weeks old. D. Adult sheep. E. Adult pig. In A and B the radial striation of the deep parts of the cortex indicates the area of vascular infiltration. The dark spot in the centre of the gland is the central vein cut across. The drawings D and E were made after the material had been fixed for some hours in Müller's fluid, the medulla thus being darkly stained.

The microscopic appearances of the suprarenal structure are very variable in the different animals studied. It will therefore be necessary to describe the phases seen in (*a*) the pig, (*b*) the lamb, and (*c*) the goat separately.

(*a*) *Pig*

In the pig at birth (see fig. 9, A) the cortex is nearly homogeneous, consisting almost entirely of large cells with vesicular nuclei and eosinophil cytoplasm. These cells are arranged in columns radiating from the centre of the gland. At first they do not show a well-marked lipoid reaction, but in 5 or 6 days this reaction is well marked in all the cortical cells. In addition to this main mass of cells there are a few very small cells underneath the capsule of the gland. They form a very narrow strip in this situation, and are not arranged in any glomerular formation. In a 3-weeks-old pig these small cells have grown to produce a definite layer about twice as thick as at birth, but still do not show a definite glomerular arrangement. They stain deeply with haematoxylin in marked contrast to the deeper cells. Their nuclei are not vesicular and their cytoplasm not markedly eosinophil. The medulla of the suprarenal of young pigs is not present in great quantity though exceeding the amount in Primates. The cortico-medullary boundary is not well marked at birth, but becomes so by the age of 3 weeks.

Vascular changes occur in the meantime, but these are not so well marked as in the lamb described below. There is an engorgement of the vessels of the main mass of the cortex and this is still seen at the 3-weeks-old stage. There are no definite haemorrhages such as are seen in the lamb and the goat.

In the adult pig the main mass of the suprarenal still consists of cortex, though this is not so hyperplastic as in the sheep (see fig. 8). The cortico-medullary boundary is very definite; though there is one large mass of cortex almost completely surrounded by medulla on account of the folding of the gland surface. The main mass of cortex consists of large eosinophil cells with vesicular nuclei and arranged in columns extending from the medulla outwards to the layer of small cells lying beneath the capsule. This layer of small cells corresponding to the glomerular zone of higher forms is about four times as thick as in the new-born pig, and does not show any definite line of demarcation from the deeper zone. On the contrary there is a tendency for the small cells to grow down between the columns of the deep layer of cortex (see fig. 9, B).

(*b*) *Lamb*

The most striking phenomena associated with the growth of the suprarenal cortex of the sheep are the vascular changes which occur immediately after birth. These vascular changes are in well-marked contrast to the condition just described above in pigs.

In the new-born lamb the suprarenal cortex consists of two main types of cells as in the pig. Immediately beneath the capsule is a very thin stratum of tiny cells staining deeply with haematoxylin. The rest of the cortex is made

up of large pale cells staining with eosin. The large cells have reticular nuclei. In the main they are arranged in columns at right angles to the gland surface, but deeper in they are more closely packed and arranged in a reticular formation. The cortico-medullary boundary is indefinite. Between the groups of cells constituting the deeper half of the cortex, the small vessels radiating into the gland tissue from the central vein are seen to be packed tightly with red blood corpuscles. The engorgement is less striking as the surface of the gland is approached.

In a lamb of 24 hours the vascular engorgement has increased and involves the whole cortex, thus giving it a radially striated appearance even to the naked eye. The engorgement is also more distinctly marked in the region where cortex and medulla come together. Here the vessels radiating outwards are seen to branch so as to allow for a twig to pass outwards between each cell column.

In a lamb of 2 days old the vascular engorgement has gone on to the extent of rupture of the vessel walls and consequent haemorrhage into the cortical tissues. In many parts the haemorrhage is extensive. There is, however, no apparent destruction of cortical tissue by this process. The cells of the main mass of cortex are still quite healthy. They have well-staining nuclei and a large bulk of cytoplasm as in the new-born lamb. The thin superficial stratum of small cells does not exhibit any change.

In a lamb of 5 weeks old all the vascular phenomena have subsided, but important cellular changes are to be seen in the cortex. The stratum of small cells under the capsule has grown to about twice its former thickness, and the cells in it have become more tightly packed, but there is no evidence of any glomerular arrangement. The main mass of cortex remains as in the previous stage, but from its deep aspect in parts of the gland a decided down-growth of cortical cells has occurred into the medulla. These cells are arranged in reticular formation. They cause the cortico-medullary boundary to maintain its original indefiniteness.

In the adult sheep the cortex of the suprarenal is of enormous thickness. The medulla is merely a soft nodule of tissue embedded in its centre. Practically the whole of this mass of cortex consists of the large cells arranged in columns. The cortico-medullary boundary is very definite and the reticular zone has obviously disappeared.

(*c*) *Goat*

In a new-born kid the microscopical characters of the suprarenal were very similar to those of the suprarenal of the lamb at the same age. Most of the gland consisted of cortex; but medulla was slightly more bulky than in the lamb. The division of the cortex into two zones was more definite than in the lamb. The superficial stratum of small cells was thicker and the cells more closely packed together, though showing no glomerular arrangement. The deeper cells forming the main mass of cortex were large, pale and eosinophil and were arranged in columns as in other forms. Between the columns the

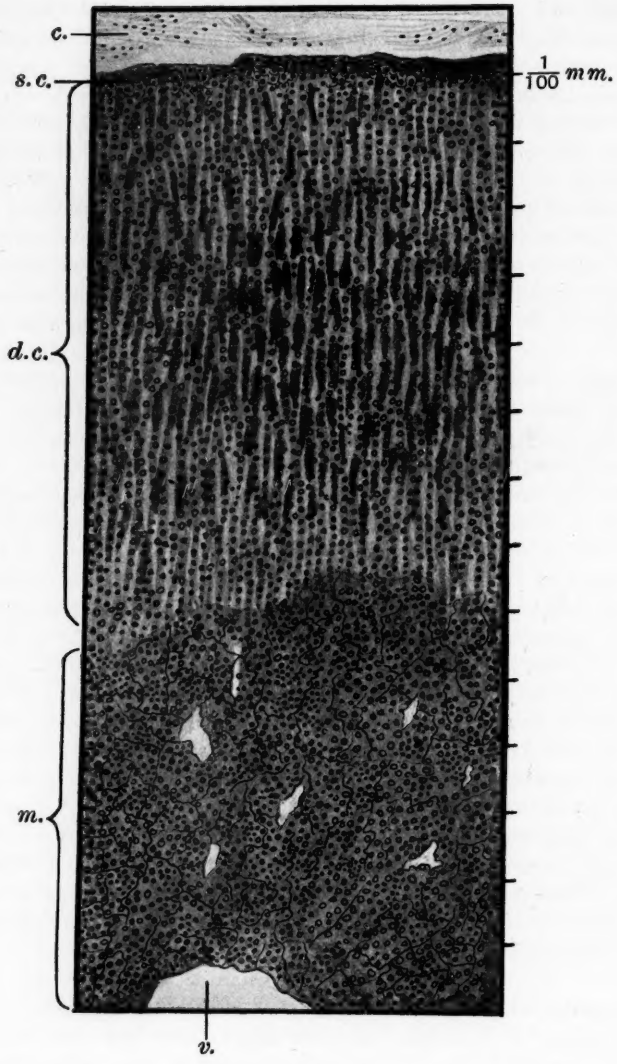


Fig. 9A. Microscopic appearances of the suprarenal of a pig, 6 days old. *c.* capsule; *s.c.* superficial cortical zone; *d.c.* deep cortical zone; *m.* medulla; *v.* central vein.

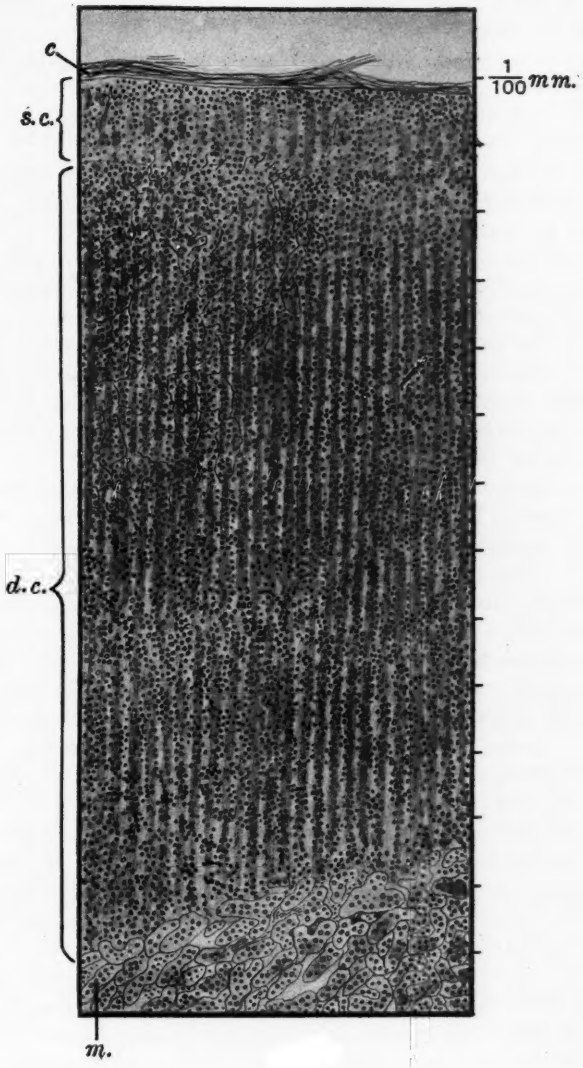


Fig. 9B. Microscopic appearances of the suprarenal of an adult pig.
c. capsule; *s.c.* superficial cortical zone; *d.c.* deep cortical zone; *m.* medulla.

radial vessels were seen in parts to be in a state of engorgement. The engorgement has in places passed on to the stage of minute haemorrhages into the cortical tissues. These haemorrhages affect both zones of cortex, but are particularly prevalent at the junction between the deep and superficial zones.

SUMMARY AND CONCLUSIONS

1. The structure of the suprarenal gland is described in young animals of the three mammalian orders, Primates, Carnivora and Ungulata, with special reference to the cortex.

2. It is shown that in all the new-born Primates examined the suprarenal presents the same size relations to the kidney as in the new-born human child; and the enlargement is shown to be due to the same factor, namely a cortical hypertrophy. In all the specimens studied the hypertrophy affects the deeper cortical layer, and is therefore comparable to the "foetal" cortex of the human foetal suprarenal. Atrophy of this zone gives the adult gland a wrinkled surface.

3. The suggestion that the lipoid reaction is of no diagnostic value in the discrimination of "foetal" cortex is confirmed.

4. The zona reticulata of the adult gland like its predecessor, the "foetal" cortex, is shown to be a transient structure, at any rate, in male Primates.

5. In mammals lower than Primates there is at the time of birth no marked enlargement of the suprarenal gland; the adult gland has as smooth a surface as the young one. In most instances, however, the relative proportions between cortex and medulla are different from those seen in the adult gland. There is always more cortex than medulla at birth. Medulla may indeed be very scanty.

6. The cortico-medullary boundary in the suprarenal of young Carnivores and Ungulates is indefinite, suggesting that some process of modification is taking place there; either an absorption of the intra-medullary islands of cortex, or a downgrowth of cortex to meet these and fuse with them.

7. The structure of the suprarenal cortex in young Carnivores and Ungulates seems to indicate that the main mass of this part of the gland consists of cells morphologically similar to those of the "foetal" cortex of Primates. The rest of the cortex consists of a peripheral rim of small cells with no uniform arrangement, but morphologically similar to the "true" cortex of Man. There is, however, no indication of an extensive degenerative process affecting the main cortical mass; hence the absence of any relative decrease in size with consequent wrinkling of the gland surface during the later stages of growth. By virtue of these facts the zone of small cells immediately beneath the capsule never emerges from its pristine undifferentiated condition as it does in Primates. One important process, however, must not be lost sight of in giving an explanation of the microscopic appearances of the cortex in young animals, and that is the phenomenon of vascular engorgement and haemorrhage. A significant fact is that the vascular changes, even when ending in haemorrhage, do not cause the destruction of any gland tissue. This remark applies equally well to

the Primate suprarenal, where the "foetal" cortex does eventually degenerate and disappear. The degeneration of foetal tissue in these forms must therefore be due to an entirely different process, and consequently another explanation must be offered for the occurrence of engorgement and haemorrhage. Possibly the increased vascularity is associated with the active growth or temporarily increased activity on the part of the main mass of the cortex. Extravasated blood in animals where haemorrhage occurs may act as pabulum for the actively growing cortical cells.

8. The zona reticulata, whenever it appears in mammals below the Primates, is shown to be a transient structure.

9. In all the animals examined the measurements show that the suprarenal is larger in female than in male animals at the time of birth.

In conclusion I wish to offer my thanks to Prof. J. C. Brash for his kindly help and criticism throughout my work; to Prof. Haswell Wilson for the use of apparatus in the Pathology Department; and to Mr H. G. Newth of the Zoology Department for one of the foetal macaques. The other foetal macaque and certain other material I have obtained through the kindness of the authorities of the Botanical Gardens, Edgbaston, Birmingham.

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A SPECIMEN OF DEVELOPMENTAL SACRO-ILIAC SYNOSTOSIS

By L. R. SHORE, M.A., M.B., M.R.C.P., D.P.H.
University of the Witwatersrand, Johannesburg, South Africa

The specimen is derived from the skeleton of a male Zulu labourer, who died in the Johannesburg Non-European Hospital at the age of 56. Death was due to acute nephritis and bronchitis; there is no record of any deformity or peculiarity of posture or gait.

The body passed through the dissecting-room of the Anatomy Department and the skeleton was prepared in the ordinary way. Fusion of the right innominate bone to the sacrum is the only abnormality in the skeleton. The joints of the limbs and of the vertebral column are free from disease.

The line of the right sacro-iliac joint is indicated in its circuit by a shallow groove which in position exactly corresponds with the edge of the sacrum on the left side. See figs. 1 and 2.

At the highest point of the right sacral ala there is a slight elevation of bone, and the groove, which elsewhere indicates the sacro-iliac joint, is obscured for about 2 cm. With this exception there is no excess of bone formation perceptible on the surface. Even quite forcible twisting movements of the two hands grasping the sacrum and the ilium fail to elicit any movement between the two bones.

A reconstruction of the pelvis was made without any difficulty. The reconstructed pelvis gives an impression of naturalness; viewed from any angle there is no deformity or asymmetry in either innominate bone or sacrum. Tracings of the reconstructed pelvis have been made by means of the dioptograph and are reproduced. Fig. 2 is a tracing of the pelvis viewed from the antero-superior aspect with the brim of the pelvis in the horizontal plane, and fig. 3 from the dorsal aspect with the dorsum of the sacrum placed vertically. The symmetry of the pelvis as illustrated in both these tracings is obvious.

The unusual character of the specimen and the absence of any sign of bony disease prompted a thorough analysis of the condition.

A section was made by means of a fretsaw in a plane intended to traverse the longest axis of the sacro-iliac joint. Guiding lines were drawn on the surface of the bone from the tubercle of the crest of the right ilium, one to the centre of the upper surface of the sacrum and another to the posterior inferior iliac spine. A cut was made in the plane defined by these two lines and continued medially into the right half of the sacrum. The portion of the ilium which lies posterior to the plane of section as defined above, together with part of the right half of the sacrum, was released by a second sawcut

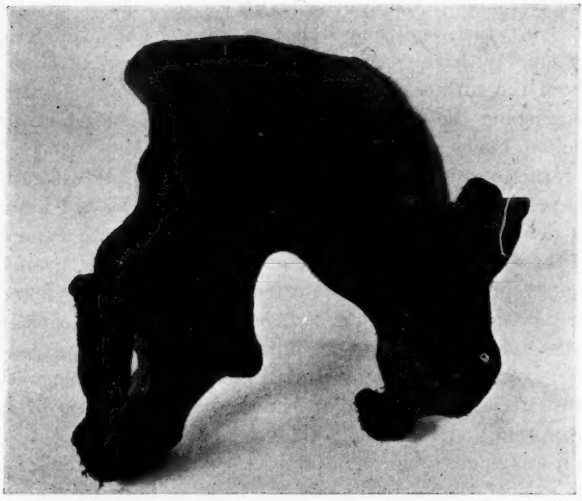

Fig. 1. In this figure are shown two photographs. *The upper photograph* shows the pelvis reconstructed and viewed from the antero-superior aspect. The general symmetry of the specimen is obvious. The position of the left sacro-iliac joint is clearly shown; in a similar position on the right side can be seen the shallow groove which indicates the union and the scanty deposit of new bone at the summit. *The lower photograph* shows the ankylosed right innominate bone and the sacrum viewed from the pelvic aspect. In both photographs the lines of section which traverse the right sacro-iliac union can be clearly seen.

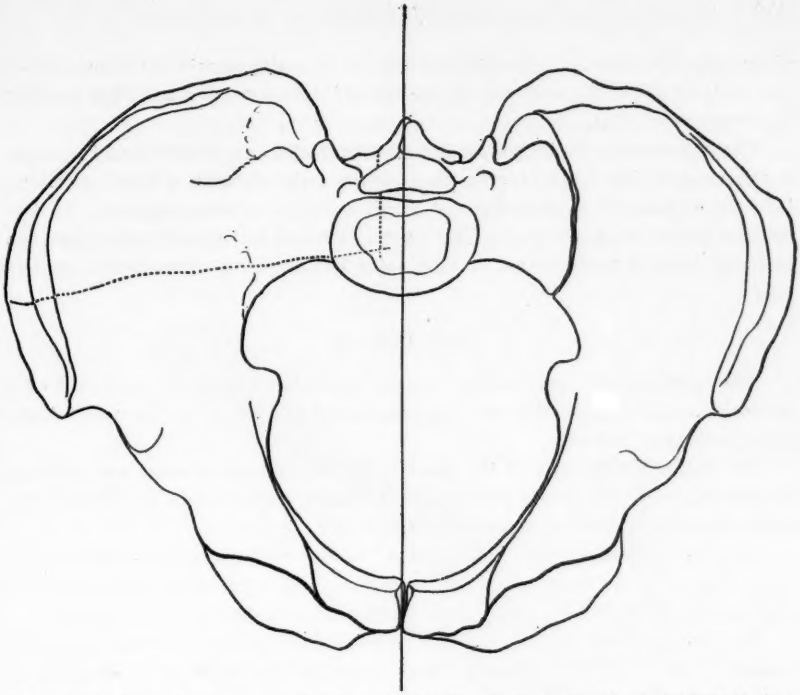

Fig. 2. A tracing of the reconstructed pelvis with the ilio-pectineal lines in the horizontal plane. The symmetry is evident. The lines of section are shown by interrupted lines. The dorsal arch of the first sacral vertebra displays the condition of spina biloba.

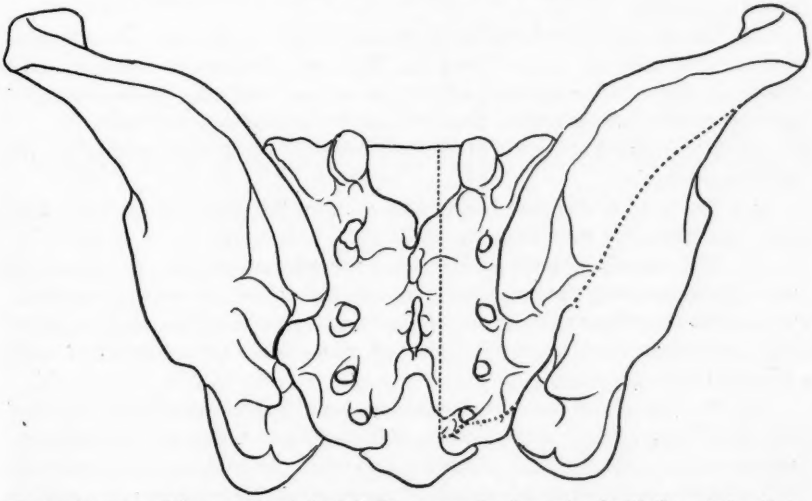

Fig. 3. A tracing of the reconstructed pelvis. The sacrum has been placed with the anterior edges of the first and fifth vertebrae in the vertical plane. The lines of section are shown by interrupted lines.

made into the sacrum from the dorsum in an antero-posterior plane about ½ in. to the right of the mid-line. These lines of section are shown in figs. 2 and 3 by interrupted lines.

The appearance presented by the cut surface of the sacrum and the ilium is recorded in fig. 4, which was prepared by rubbing with a hard pencil on thin paper pressed against the cut surface of the smaller segment. In the interpretation of a rubbing of this sort, it must be remembered that the compact bone is represented by dark lines and the cancellous spaces are left white.

DISCUSSION

The question obviously arises: Is the condition described the result of a developmental abnormality or of a pathological process of the nature of acute or sub-acute arthritis?

The following features of the specimen presented on external and internal examination suggest developmental abnormality rather than arthritis as the cause of the ankylosis between the sacrum and the ilium.

(1) The symmetry and "naturalness" of the whole pelvis are remarkable. Some degree of deformity or asymmetry would be expected to develop in the course of arthritis sufficiently extensive to obliterate the sacro-iliac joint.

(2) The position of the sacro-iliac joint on the surface is for the most part indicated by a shallow groove. There are only the slightest indications of excess bone formation.

The appearances presented at the surface of a joint which has undergone ankylosis as a result of inflammation would certainly include abnormal outgrowth of bone.

(3) The section reproduced in fig. 4 shows very clearly that synostosis is complete in the long axis of the joint. This completeness of compact bony fusion in the interior of the joint is inconsistent with the scanty bone of spongy nature thrown out on the exterior, if the process is inflammatory.

(4) The internal structure of the bone as shown in fig. 4 presents several significant points:

(*a*) The band of compact bone which replaces the cavity of the sacro-iliac joint is remarkably even in width.

(*b*) The cancellous bone of the ilium presents no change in its texture when followed along the sacro-iliac junction from pelvic brim to sacro-sciatic notch. The cancellous spaces are of approximately the same size and no pathological process either in the direction of excess bone formation or of bone absorption is suggested.

(*c*) The cancellous tissue of the sacrum is not so well displayed as that of the ilium. The process of sectioning with the fretsaw was not successful in producing an absolutely level surface. As a result the rubbing lacks definition in places where the finer bony plates have broken. Nevertheless, the surface displayed gives no evidence of pathological change. Examination of the actual

cut surface of bone leads to the same conclusion, viz., there is no evidence either of excess bone formation or of bone absorption.

It is the uniformity which really compels acceptance of developmental synostosis as the explanation. Uniformity in the extent of the union, uniformity in the compact bone which replaces the sacro-iliac joint and uniformity in the texture of the cancellous bone which abuts on the union are together and severally inconceivable as the result of synostosis of arthritic origin.

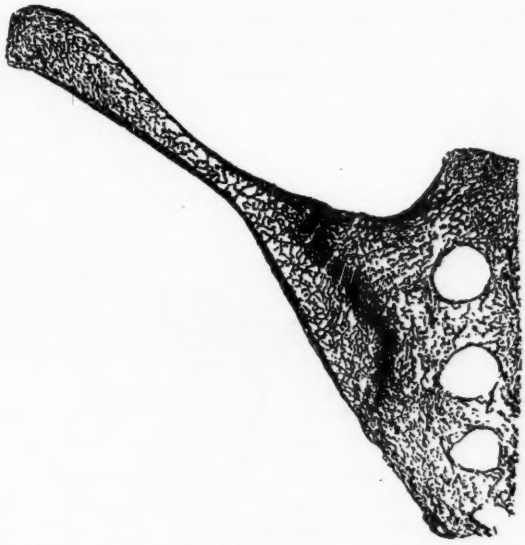

Fig. 4. A rubbing taken from the surface of bone revealed by section in the planes indicated in the foregoing figures. Compact bone is represented by dark lines and cancellous spaces are left white. The dark band in the position of the sacro-iliac joint is clearly shown. The even width of this band of compact bone and the uniformity of texture of the cancellous bone on either side of this band are specially to be observed.

Strangely enough, a second specimen of sacro-iliac ankylosis was secured amongst the next few skeletons prepared in this Department. Examination of this specimen, in which ankylosis was certainly due to pathological processes, provides points of contrast with the specimen already described, not only in external appearances but also in the features of internal structure revealed by section. This second specimen is derived from a male of mixed race aged 90 and is also on the right side.

When viewed from the abdominal aspect irregular projections of bone can be seen to unite the upper part of the right sacral ala to the venter ilii, completely obscuring the sacro-iliac joint. From the pelvic aspect, however, it seems that ankylosis is incomplete; a deep cleft separates the sacrum and the

ilium, 5 mm. wide at the great sacro-sciatic notch. On the dorsum the joint is also marked by a cleft, for two-thirds of its length. In spite of these deficiencies the sacrum and the ilium are firmly united to each other, and the union resists the exercise of very considerable twisting force applied by the two hands. The vertebral column corresponding to this second specimen presents evidence of some pathological process in numerous exostoses on the margins of the vertebral bodies and on the circumference of many of the small joints of the vertebral column. Osteo-arthritis of the larger joints of the upper and lower limbs had been noted during life and is evident in the skeleton. These other evidences of disease combined with the exostoses at the sacro-iliac joint and a lack of uniformity in the degree of ankylosis go far to proclaim the nature of the condition as pathological.

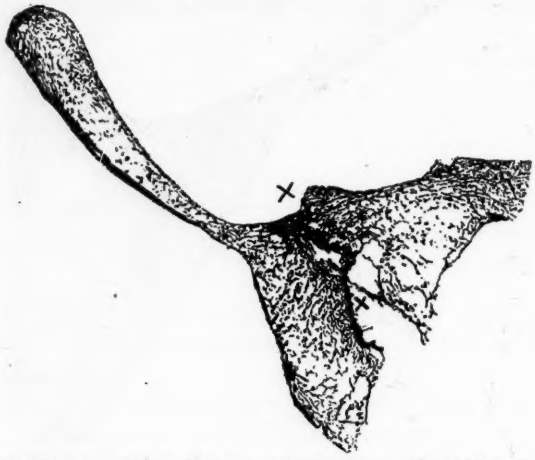

Fig. 5. A rubbing taken from the surface presented by section through the sacro-iliac joint of a specimen in which union is certainly pathological. The plane of section is not exactly the same as that shown in fig. 4. The position of the joint lies between the points *X* and *X*. Note the joint cavity is not quite obliterated and the compact bone between *X* and *X* is not uniform either in width or texture, neither is the texture of the cancellous bone at the sides of the joint uniform.

In making a section I failed in my intention to traverse the sacro-iliac joint in its longest axis. It proved impossible to repeat the attempt because the union broke in handling and it was revealed that bony union was limited to the upper part of the joint and that ankylosis was fibrous for the most part. This finding surprised me, because, having handled the joined sacrum and ilium, I should not have expected such stability apart from bony union.

The section has, however, traversed the superior or vertical limb of the sacro-iliac joint for about an inch, and the rubbing made sufficiently illustrates the appearances presented by synostosis consequent on inflammation. In fig. 5 the sacro-iliac joint lies between the points *X*——*X*. The following

features may be discerned and may be contrasted with the findings revealed by section traversing the site of the right sacro-iliac joint of my first specimen.

(1) The cavity of the joint is only partly obliterated.

(2) The compact bone about the joint, both in the sacrum and in the ilium, is uneven in its thickness. The layer of compact bone is thickest at the superior extremity of the joint and narrowest at the lower extremity.

(3) The cancellous bone around the joint is also uneven in its texture. Strands of compact bone invade the cancellous tissue of both bones, especially near the upper part of the joint, and contribute to the unevenness of texture. Any general tendency exhibited by the cancellous bone is in the direction of rarefaction rather than of condensation.

(4) It might be surmised that the seat of incidence of the disease was in the upper part of the joint, where synostosis is most complete and where condensation of the cancellous bone indicates the greatest tissue reaction.

THE OCCURRENCE OF SACRO-ILIAC SYNOSTOSIS

It is difficult to form an estimate of the frequency with which developmental synostosis of the sacrum and the ilium occurs.

The Museum of the Anatomy Department of the University of the Witwatersrand contains this single specimen in 101 Bantu skeletons. I should, however, judge the condition to be very much rarer than this proportion would suggest.

The literature at my disposal contains scarcely a reference to developmental synostosis of the sacrum and the ilium. The condition is not mentioned in six text-books of Anatomy, those of Cunningham, Gray, Macalister, Morris, Piersol and Quain. Nor has the condition been recorded in the *Journal of Anatomy* since 1918, in the *Anatomical Record* since 1906 or in the *Folia Anatomica Japonica* since 1922. Search in the *Lancet* and the *British Medical Journal* has also led to a negative result.

Humphry (1) briefly mentions ankylosis of the sacro-iliac joint in a clinical note on the symphysis pubis, which, he states, "is rarely the seat of ankylosis. A case is related by Otto (de rariori quodam pleniariae pubis ankylosis exemplo) where it, as well as the right sacro-iliac joint, was completely ossified in a woman aged 32.... In the sacro-iliac joint, on the contrary,...ankylosis is of more common occurrence." Humphry evidently considers ankylosis of the sacro-iliac joint less rare than a like condition of the symphysis pubis. I have no closer reference to the writings of Otto and no opportunity of consulting this author. It is not clear if Otto is referring to developmental or to pathological ankylosis, but the completeness of the ossifications suggests developmental ankylosis in a young woman. Association with ankylosis at the symphysis pubis gives no definite indication in the choice of alternatives, but it seems to me that two abnormalities of the same order in the same individual tend rather to strengthen the view of developmental origin. Even if it were

shown that this case of Otto's were pathological, it would still have to be regarded as one of great rarity.

Bony ankylosis of either origin is an uncommon condition, as is shown by Brooke(2), who made a study of the sacro-iliac joint with a special view to its mobility and the relation of mobility to age and liability to pathological conditions. Although ankylosis is recorded in 37 per cent. of male sacro-iliac joints of all ages, in every case ankylosis is by fibrous tissue; no mention is made of ankylosis by bone, whether developmental or pathological.

Le Double(3) considers unilateral ankylosis of the sacrum, more or less complete, as a common occurrence but is evidently referring to the pathological condition.

In another place Le Double(4) expresses an opinion regarding deformity of the pelvis as an accompaniment of unilateral sacro-iliac ankylosis. In discussing the so-called "Naegele" pelvis or "bassin oblique ovalaire," of which the cause is attributed by Naegele to unilateral sacro-iliac ankylosis, Le Double demands in addition "une rudimentation plus ou moins accentué d'une des moitiés latérales du sacrum."

The exact symmetry of the pelvis in my specimen of non-pathological synostosis affords the clearest evidence that fusion took place after the period of full growth. The "Naegele" pelvis illustrated by Le Double(5) shows a narrowing of the sacral ala on the side of fusion and a reduction of size and spread of the ilium on the same side. The inference is that in the "Naegele" pelvis synostosis took place early in the growth period.

In short, my specimen differs from the "Naegele" pelvis chiefly in the date of fusion. There seems no reason why fusion after full growth should be associated with asymmetry, while fusion in early life would be expected to result in asymmetry and obliquity. Le Double considers the "Naegele" pelvis to be an excessively rare condition and remarks that the specimens of sacro-iliac ankylosis in the Musée Dupuytren, to the number of ten, are all associated with perfectly normal sacra and symmetrical pelves. Le Double, however, gives no indication of the frequency of occurrence of sacro-iliac ankylosis.

The nature of the stimulus which has induced bony fusion such as that described is beyond my conjecture. I imagine, however, that the stimulus, in this case, as it were, misapplied, is not different in kind from that which normally induces the fusion of an epiphysis or of the vertebral components of the sacrum. The term "congenital" is inapplicable if we accept the deduction that fusion took place after full growth, for the condition cannot date from birth. I have therefore preferred the term "developmental" or non-pathological to indicate the nature of the synostosis.

A feature of my specimen of developmental or non-pathological synostosis which surprised me is the persistence of a band of compact bone between the sacrum and the ilium in an adult of advanced years. Zachary Cope(6) has pointed out that an epiphyseal junction may be marked by a band of compact

bone many years after union of the epiphysis, even into the sixth decade and after. The band of compact bone in this specimen is 5 mm. wide, far wider than in the examples furnished by Zachary Cope.

Commonly, the compact band marking an epiphyseal line is obliterated at last by the spread of cancellous cavities across the site of union. I have observed the same phenomenon in connection with pathological synostosis. Sections through joints which are ankylosed, definitely as the result of inflammation, often show the continuity of cancellous cavities across the site of bony union.

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A DESCRIPTION OF THE EGG TOOTH OF *ORNITHORHYNCHUS*, TOGETHER WITH SOME NOTES ON THE DEVELOPMENT OF THE PALATINE PROCESSES OF THE PREMAXILLAE

By H. L. GREEN

Demonstrator of Anatomy in the University of Cambridge

In 1865 Owen (3) drew attention to the presence of a dorsally situated caruncle on the snout of the young of *Ornithorhynchus*; later, W. N. Parker (4) described a similar structure in young *Echidna* embryos and referred to it as an "egg breaker" or "Eischwiele." Though this structure is almost certainly homologous with the "Eischwiele" of birds, crocodiles and tortoises, Semon's (7) pictures of various *Echidna* embryos, at younger stages than had previously been described, clearly show that the two structures cannot be analogous. In these embryos, in addition to the caruncle, an undoubted "egg breaker" could be seen situated on the ventral aspect of the snout in the mid-line and projecting from under cover of the upper lip. Seydel (8) investigated the structure of this egg tooth at various stages in *Echidna* and described his findings in some detail.

Although the presence of a similar structure has been surmised for *Ornithorhynchus*, I do not think it has ever been described, probably because suitable stages are extremely difficult to acquire. Through the kindness of Prof. J. T. Wilson I have been able to examine a series of sections of a young *Platypus* embryo in his collection (originally procured by Prof. J. P. Hill) which fortunately demonstrates the characters of a fully mature egg tooth, and it seemed advisable that an account of its structure should be placed on record.

The embryo is catalogued as Specimen "W" and it had the following measurements:

Maximum "direct" length	16·5 mm.
Head length	6·0 mm.
Total length (as measured along the dorsal surface from the tip of the snout to the tip of the tail) ...	28·0 mm.

Fig. 1 illustrates its general appearance.

One of its most striking features is the enormous caruncle which forms the raised swelling on the dorsum of the snout. The egg tooth proper appears as an unpaired, conical, peg-like projection pointing directly downwards from the mid-line and situated a short distance behind the anterior end of the upper jaw. Its point is quite free and projects outside the tip of the lower jaw.

The specimen was embedded in paraffin and cut into serial sections (10 μ) transversely to the trunk; the plane of section was therefore, as may be seen from the illustration, oblique to the snout region. The sections were stained in haematoxylin and eosin.

On examination the premaxillary bones are found to be relatively very extensive, as they are specialised at this stage not only to constitute dorsally the massive "os carunculae" but also to carry, on their ventral aspect, the egg tooth. The base of attachment of this egg tooth extends antero-posteriorly over 32 sections, i.e. a third of a millimetre, which is a very appreciable portion of the whole head length (6 mm.). The os carunculae is found as a fusion of the anterior ends of the two premaxillae as they turn up dorsally in front of the forward extremities of the cartilaginous nasal capsule. From this upturned dorsal fusion the palatine trabeculae of the premaxillae can be followed back on either side of the mid-line, ventral to the cartilaginous nasal floor (fig. 2, section A), until a point is reached (fig. 2, section B) where they again fuse across the mid-line (Seydel's "vordere Verbindung" in *Echidna*); this corresponds to the anterior limit of the base of attachment of the egg tooth. It is worthy of note that in the older specimens modelled by Wilson (15) there remains no trace of such a union between the ventral parts of the premaxillae.

A few sections farther back the ventral premaxillary trabeculae split on either side into a medial and a lateral lamina. It is the lateral lamina which corresponds to the "ventral lamella" of the body of the premaxilla described by Wilson. The medial lamina is represented in later stages, at least in part, by the "palatine process." The medial lamina is vertically, while the lateral lamina is horizontally, flattened. They are continuous along the lower margin of the medial lamina except where they are separated by a large vascular foramen (fig. 2, section C) and also for a short distance posteriorly where the hinder end of the medial lamina projects backwards as a free, though at this stage short, palatine projection (fig. 2, section F). Here also the medial laminae of opposite sides again show an area of fusion (fig. 2, section E) corresponding to the posterior limit of attachment of the egg tooth. The palatine processes of the premaxillae are continued back beyond this area of fusion for only about 50 μ. They are closely applied on either side to the ventral aspect of the anterior ends of the cartilage of Jacobson's organ.

The main substance of the tooth itself consists of a calcified shell in the shape of a hollow cone curved backwards in cornuate fashion, the hollow being filled by loose mesodermal tissue forming an extensive "pulp cavity." The precise structure of the hard substance which forms the shell of the tooth is indeterminate. It is apparently identical with that of the corresponding structure in *Echidna* as set forth by Seydel. All one can recognise is this cone-shaped layer of calcification which, as far as can be seen, is entirely homogeneous and which exactly resembles the structure of the premaxillary trabeculae except that it has a slight preference for the basic haematoxylin stain as

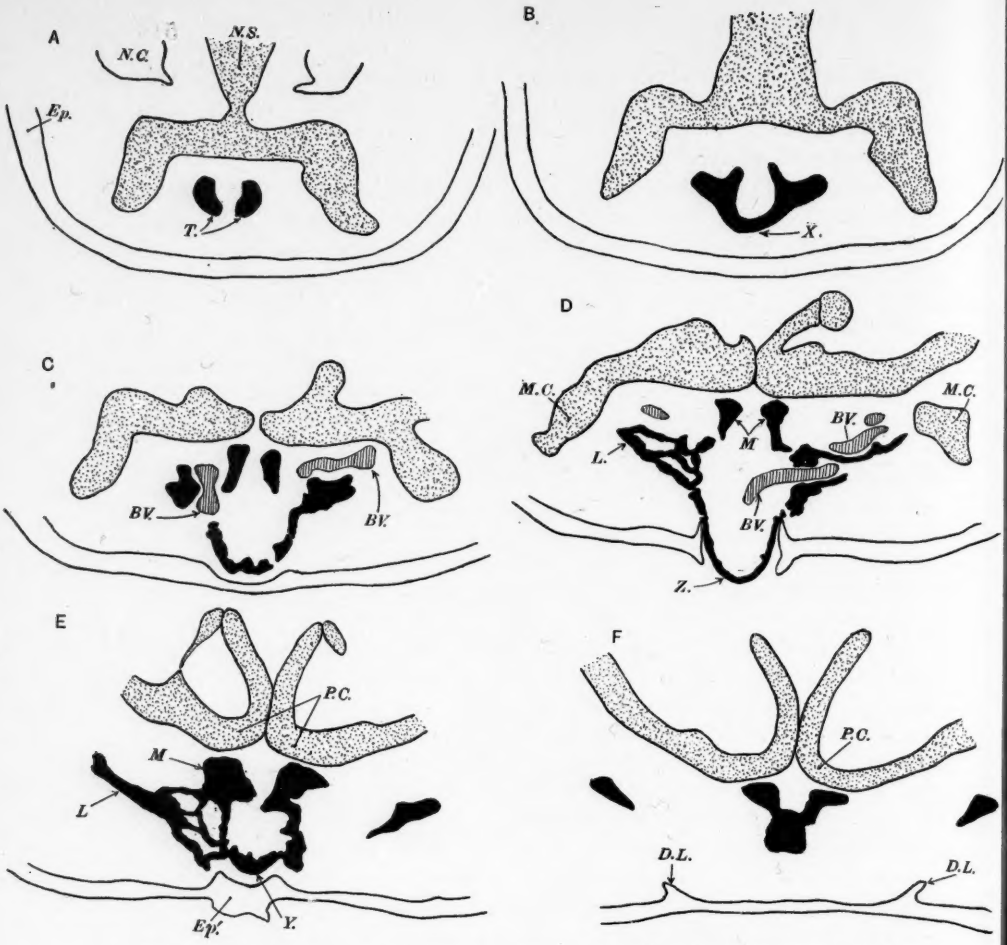

Fig. 2. A series of six sections (× 58) through the snout region of specimen "W" to show the general relations and structure of the egg tooth and the related parts of the premaxillae. The sections are arranged in antero-posterior sequence from A to F. The average distance between sections is 80 μ.

The epithelium of the upper jaw is left white, the cartilage is stippled and the premaxillae and the egg tooth are in black.

Section D is a diagrammatic representation of the same section as that from which the photograph in Fig. 3 was taken.

BV. The large blood vessels which enter the "pulp cavity" of the egg tooth between the two laminae of the premaxillae. *D.L.* The anterior end of the dental lamina. *Ep.* Epithelium of the upper jaw. *Ep.'* A heaping up of the epithelium as it again becomes continuous behind the point where it is perforated by the egg tooth. *L.* Lateral lamina of the premaxilla. *M.* Medial lamina of the premaxilla. *M.C.* The marginal cartilage. *N.C.* Nasal cavity. *N.S.* Cartilaginous nasal septum. *P.C.* Paraseptal cartilage. *T.* Trabeculae of the premaxillae leading back from the os carunculae. *X.* Anterior area of fusion of the premaxillae. *Y.* Posterior area of fusion of the premaxillae. *Z.* "Dentinal" shell of the egg tooth projecting through the epithelium.

opposed to the acidophile reaction of the bony tissue proper. The outer aspect is smooth and has some scattered remnants of epithelial cells still adhering to it. The inner surface, which is apposed to the mesodermal tissue of the papilla, is more irregular, though a great part of this may be accounted for by secondary osteoclastic absorption. Whether or not this tissue can be called dentine is problematic: as no cells are visible in its substance (which is homogeneous as previously stated) it is presumably some form of osteodentine.

The oval base of the tooth is, at the stage described, fused with the premaxillae at the junction of the medial and the lateral laminae, the area of attachment extending from the region of premaxillary fusion shown in fig. 2, section B, to the posterior fusion shown in fig. 2, section E. No exact line of structural demarcation between the tooth and the bony tissue of the premaxillae could be detected.

An idea of the general relations of the tooth can be gained by a study of fig. 3, which represents a photograph of the same section as that from which section D, fig. 2, was drawn.

The tooth is seen projecting through the epithelium of the upper jaw. The medial and lateral laminae of the premaxillae are seen to be continuous with each other and with the base of the tooth on either side. The medial lamina is slightly flattened on its dorsal surface and is applied to the under aspect of the capsule of Jacobson's organ, the anterior end of which is clearly seen cut in this section. The lateral lamina lies more ventrally and reaches outwards as far as the marginal cartilage of the jaw where it doubtless represents the ventral moiety of the later premaxillary body.

At no point can any specialisation of the epithelium overlying the tooth be noticed; it is not particularly thickened nor are its basal cells modified or arranged in any particular way so as to suggest the presence of an "enamel epithelium." It is noticeable, however, that at the point of breaking through of the tooth the epithelium surrounding it sinks deeply into the tissues (fig. 4, *X*), perhaps indicating that, were earlier stages available, the epithelium might be found to take some part in the formation of the tooth. Nevertheless, though such an epithelial activity was surmised by Seydel, who examined earlier stages in *Echidna*, no trace of enamel can be found covering any part of the external aspect of the tooth.

It is impossible also with the material available to decide whether or not this egg tooth arises close to the epithelium independently of the premaxillae and later fuses with them. Almost certainly the tooth arises independently, as Seydel has shown that it does in *Echidna*. In some sections indeed there seems to be a region of union fairly clearly demarcated which would correspond to the "bone of attachment" of the tooth.

Just in front of the hinder end of the base of the tooth the lateral laminae are found to separate from the palatine processes. It is significant that at this point also the anterior end of the dental lamina appears as a short oblique ingrowth from the epithelium of the upper jaw, directed towards the freed

parts of the lateral laminae. From its position in relation to the dental lamina the egg tooth might perhaps therefore be regarded as in series with the developing true teeth.

The tooth as a whole, though still a prominent structure, has undoubtedly passed its prime and is being absorbed. This is an extremely active process as is shown by two facts:

1. In the sections described there is a remarkable demonstration of osteoclastic activity. Throughout the tooth region large numbers of multinucleated giant cells with the nuclei arranged around the periphery of the cell are present in the mesoderm. They lie in recesses on the deep surface of the dentinal shell and particularly around the region of the "bone of attachment" of the tooth. In addition, there is a very pronounced vascularity in this neighbourhood, the vessels being both numerous and of large calibre; cf. fig. 4 and fig. 2, sections C and D.

2. In specimen "X," which belongs to Prof. J. P. Hill's collection and which he kindly allowed me to examine, there is no sign of a break in the continuity of the mouth epithelium and all trace of transverse connections between the palatine processes of the premaxillae has vanished. The specimen measured 56 mm. along the dorsal contour of the body from the tip of the snout to the tip of the tail.

DISCUSSION ON THE NATURE OF THE EGG TOOTH

As regards the nature of this egg tooth, it is clear that it is homologous with the corresponding structure in *Echidna*. It is equally clear that the monotreme egg tooth is not to be compared with any other known eggshell-breaking apparatus, except of course from the point of view of function. The "Eischwiele" of birds, crocodiles and tortoises is a purely epidermal structure, while the egg teeth ("Eizähne") of the lizards and snakes are simply the two most anterior elements (one on either side) of the ordinary dentition of the upper jaw, specialised for the purpose of breaking the eggshell by being developed much more rapidly than the remaining teeth and also by being directed forwards instead of downwards. This latter type of egg tooth is in fact developed in the depths of the tissues of the jaw from a dental lamina.

It is highly improbable that the egg tooth in *Ornithorhynchus* is developed from a dental lamina: it is large, already fully calcified and even in the stage of absorption, while the dental lamina is in a very early stage of its ontogenetic history. In specimen "W" the dental lamina is a continuous epithelial downgrowth, slightly swollen here and there, but as yet not even showing any definite mesodermal indentations to indicate the situation of the future enamel organs. Again, the early history of the tooth has been observed in *Echidna* (8), and here it arises on the apex of a mesodermal papilla, immediately on the deep aspect of the mouth epithelium.

In its form and general relationship to other tissues this tooth entirely resembles the dentinal shell described by Wilson and Hill (16) as an undoubted remnant of a milk tooth (*dv*) of *Ornithorhynchus* (fig. 5).

The tooth *dv* is developed immediately under the epithelium, not apparently involving the necessary antecedent development of the dental lamina which appears on its lingual side and produces a later dentition. The relation of *dv* to the lamina is certainly less intimate than that of the typical mammalian milk tooth to its parent lamina. It might well represent an early phylogenetic stage of tooth evolution, a stage between that shown by a typical placoid scale which is developed on a mesodermal papilla immediately under the epithelium and that in which a dental lamina is formed and teeth are produced in the depths of the mesoderm at some distance from the deep surface of the epithelium.

The crocodiles present for examination just such an intermediate stage in the progress of tooth evolution. Röse (5) found that the earliest teeth to be developed in the crocodiles are formed as quite superficial structures independently of the dental lamina which will succeed at a later stage of ontogeny. These teeth are absorbed before reaching maturity, but there is no doubt as to their presence which I have been able to confirm by examining a series of sections of a young crocodile embryo. Several of these very early teeth are seen developing around the margins of both upper and lower jaws before there is any sign of the formation of a dental lamina. A photograph of one of these denticles is reproduced in fig. 6 because I think it can be taken to represent what probably was an earlier stage in the development of the egg tooth of the monotremes. A thin dentinal shell is laid down between the epithelium and the mesoderm. The latter is condensed and raised up to form a definite papilla which pushes the epithelium in front of it. In fact at this stage it might represent a developing selachian denticle. If this dentinal cap increased in size and fused at its base with the underlying premaxillae and if its point penetrated the overlying epidermis, we should have exactly the condition realised in the mature egg tooth of *Ornithorhynchus*.

The monotreme egg tooth, therefore, structurally represents an extremely old phylogenetic type of tooth evolution.

THE PALATINE PROCESSES OF THE PREMAXILLAE

At this early stage of development it is found that a large egg tooth is present in *Ornithorhynchus* and is carried entirely on a premaxillary base. After the embryo has left the egg, the tooth of course becomes functionless and in a short time is wholly absorbed by the action of phagocytic cells. This process of absorption involves the tooth itself first of all and later spreads to the parts of the premaxillae to which the base of the tooth is attached. From

the extent, in this specimen, of the medial laminae of the ventral premaxillary trabeculae and their short posterior prolongations, the palatine processes, it is clear that their main if not their sole function is to support the egg tooth. One might expect therefore that, with the disappearance of the tooth on hatching from the egg, these parts of the premaxillae would undergo reduction and gradually be absorbed. As will be seen, however, this reduction, although it does occur later, is not coincident with or even immediately consequent upon the loss of the egg tooth as might have been expected.

I have been able to examine the course of development of the palatine processes in a limited number of later stages though, even so, the stages are not sufficiently close to allow an absolute decision on the origin of the "prevomers" or "dumb-bell bone" to be made. Certain new facts have however come to light.

Symington (10) held the view that the dumb-bell bone represented the detached and fused posterior ends of the palatine processes. Wilson (15) denied this and recognised the bone as a distinct "prevomerine" element arising from a bilateral centre of ossification at a later ontogenetic stage than the palatine processes of the premaxillae. This he assumed on the grounds that, by comparison of the two specimens available to him at that time, the younger one showed palatine processes and no "prevomers," while the older one still showed the palatine processes, the same length as in the younger specimen, and, posterior to them and separated by a considerable interval (1 mm.), had appeared the "prevomers" ventral to Jacobson's organ. He drew the conclusion from this that the palatine processes were regressing or at least had remained stationary and new ossifications had arisen posteriorly.

Recently Prof. Wilson was good enough to lend me a specimen of *Ornithorhynchus* at a stage about midway between the two he had described. This was his specimen XXVIII B, with a snout–tail measurement of 122 mm. His two specimens mentioned above measured 80 mm. and 250 mm. respectively. I embedded the head of this embryo in celloidin and cut it into serial sections at 50 μ transversely to the snout. The sections were stained in haematoxylin and eosin.

Examination of the snout region of this embryo revealed an interesting state of affairs with regard to the palatine processes of the premaxillae. On tracing them posteriorly each was found to dwindle away to a mere thread of ossification just anterior to the front end of the paraseptal cartilage: this thread is traceable back to a point 0·25 mm. behind the anterior extremity of the cartilage, where it suddenly widens out into a thin plate of bone which is placed immediately ventral to the paraseptal cartilage and which extends posteriorly for a distance of about 0·4 mm. This thin, horizontally flattened plate of bone (which is bilaterally situated though the bones of both sides are enclosed in a common sheath of condensed mesenchymatous tissue) is in all respects comparable to and is obviously homologous with the "prevomerine" elements which appear as separate entities at a rather later stage. If this is

the case, it seems as though the dumb-bell bone is merely a detached piece of the palatine processes of the premaxillae. Apparently the very thin thread of ossification which in this specimen acts as a connecting link between the anteriorly situated palatine processes and the posteriorly situated "prevomer" is undergoing a process of absorption, thus leading directly to the condition described and modelled by Wilson in his older embryo where the palatine process is quite separate from the dumb-bell bone. As is to be expected, this line of ossification does not extend so far in a posterior direction in specimen XXVIII B as in the older stage of Wilson's; this, however, is only an early stage in what is an active backward growth of these elements. Wilson mentions in his paper that the dumb-bell bone does not extend so far posteriorly in the stage he describes as it does in the adult, where it reaches the roof of the internasal aperture. Stages in the growth in length of the palatine processes are shown in fig. 7; the diagrams are drawn strictly to scale from the respective embryos.

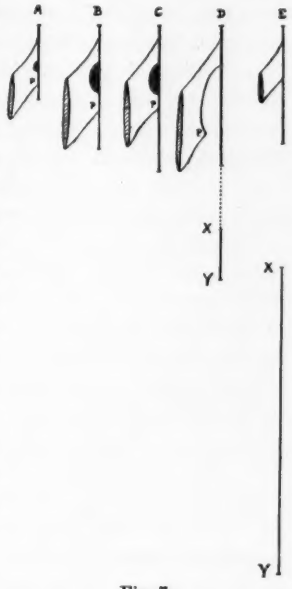

Fig. 7.

Fig. 7. A diagram to illustrate the relative lengths of the palatine processes of the premaxillae of *Ornithorhynchus* at various stages. The respective curved snout–tail lengths of the embryos were as follows: A, 28 mm.; B, 56 mm.; C, 80 mm.; D, 122 mm.; E, 250 mm.

The upper ends of the lines represent the anterior ends of the premaxillae where these turn dorsally as the "os carunculae." The flange of bone shown cut across in each case is the lateral lamina; in A, B and C this is seen to be attached to the medial lamina by two processes (the posterior of which is marked *P*) separated by the vascular foramen which is shown in fig. 2, section C.

In D the dotted line represents that portion of the palatine process which is referred to in the text as "a thin thread of ossification": it will be noticed that the corresponding area in E is left blank, the line of ossification having disappeared at this stage.

X–Y is that part of the palatine process which will become the dumb-bell bone of the adult skull.

The reduction of the anterior ends of the palatine processes seems to depend eventually upon the loss of the egg tooth; when this disappears a gradual reduction in the extent of the posterior union of the medial and lateral laminae of the premaxilla occurs. This union at last fails entirely, as in XXVIII B, and as a result the anterior parts of the palatine processes dwindle into insignificance while the posterior portions are retained to act as supports for or as protections to the paraseptal cartilages.

It is clear, therefore, that now this intermediate stage is available, Wilson's statement (15) that "it is evident that the prevomerine dumb-bell arises auto-

genously during the interval in development between the stages illustrated by Models i and ii, and is from the beginning separated by a wide interval from the true palatine process of the premaxilla" can no longer be held to be accurate. His stages were too remote from each other, as it happens, to justify this surmise. It is interesting to note that that part of the palatine processes which is extremely attenuated in specimen XXVIII B corresponds exactly in position to the gap between the palatine processes and the dumb-bell bone in Wilson's specimen.

Since this was written de Beer(2) has published his paper on the development of the skull of the shrew. In it he expresses his views on the homologies of the palatine processes of the premaxillae and the prevomers. He recognises three stages in the phylogeny of these structures. First, the complete separation of the premaxillae and prevomers as in reptiles. Secondly, intermediate stages in which the premaxillae send back palatine processes towards the prevomers to strengthen the efficiency of the latter as supporting structures; this stage is subdivided, *Ornithorhynchus* showing the commencing growth back of the palatine processes, these not actually reaching the prevomers (dumb-bell bone), while in some higher Mammals the processes fuse on to the prevomers, though the latter still express their individuality by retaining separate centres of ossification ("anterior vomers"). Thirdly, the stage of the remaining Mammals in which the prevomers are completely incorporated (as de Beer's "prevomerine process") in the apparent palatine processes of the premaxillae and no longer show separate ossification.

If further investigations should corroborate what has been found in specimen XXVIII B, *Ornithorhynchus* can no longer be held to occupy the intermediate position in which de Beer places it in his scheme. There is as yet no positive evidence that the dumb-bell bone arises from a separate centre of ossification, despite the fact that its probable phylogenetic history as outlined by de Beer indicates that it should do so. A specimen slightly younger than XXVIII B might show an independent prevomerine centre but in any case it seems that a stage of continuity follows, after which separation of the two elements occurs.

Examination of further material is necessary before dogmatic statements can be made, but it certainly appears that the conditions in *Ornithorhynchus* are not quite so simple as would be required to fit it into the position assigned to it by de Beer: the later, obvious separation of the palatine processes of the premaxillae and the dumb-bell bone is secondary to a short stage of continuity and is not a primary condition as has been thought.

SUMMARY

1. The structure of the mature egg tooth of *Ornithorhynchus* is described and compared with that of *Echidna*.

2. Reasons are given for believing that this tooth represents a very early phylogenetic stage of tooth formation.

3. The course of development of the palatine processes of the premaxillae is given so far as material has been available.

4. The origin of the dumb-bell bone is discussed and it is suggested that its origin as a distinct prevomerine element is yet to be proved in the case of *Ornithorhynchus*.

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EXPLANATION OF PLATE

Fig. 1. A photograph of *Ornithorhynchus*, Specimen "W," before sectioning. × 3·6. The egg tooth is seen projecting from under cover of the upper jaw at *A*. The large dorsally placed caruncle is seen at *B*.

Fig. 3. A photograph of a section to show the general relations of the egg tooth. × 35.

A. Cartilage of the nasal septum. *B*. Nasal cavity. *C*. The anterior end of the cartilage of Jacobson's organ. *D*. Marginal cartilage of the jaw. *E*. Egg tooth projecting through the epithelium.

Fig. 4. A photograph of the egg tooth region in the same section as that represented in fig. 3. × 100.

A. The "dentinal" shell of the tooth. *B*. Some of the multinucleated giant cells in this region. *C*. The medial lamina of the premaxilla. *D*. The lateral lamina. *X*. The infolding of epithelium around the base of the tooth.

Fig. 5. A photograph of Wilson and Hill's calcified vestigial milk tooth *dv* in the upper jaw of a foetal *Ornithorhynchus*. × 100.

Its intimate relation to the epithelium of the mouth is well shown; the dental lamina is seen on its lingual side.

Fig. 6. A photograph of one of the denticles in the early transitory dentition of a young crocodile embryo. A thin shell of dentine is seen lying on the surface of the condensed mesodermal papilla, immediately underneath the mouth epithelium. × 200.

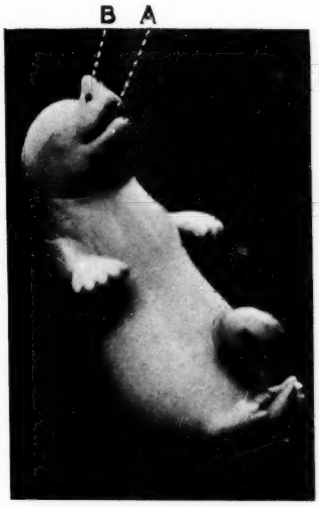

Fig. 1

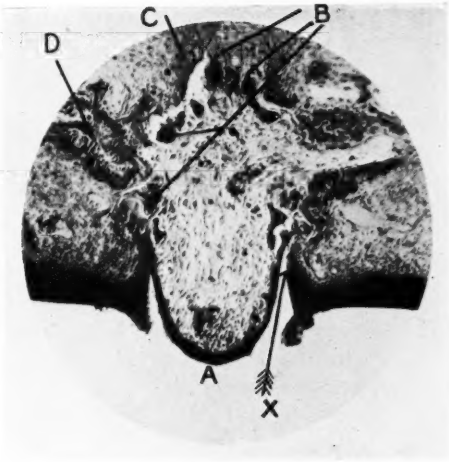

Fig. 4

Fig. 5

Fig. 3

Fig. 6

UNIV. OF MICH.

A CASE OF HUMAN DIPHALLUS

By CHARLES DONALD, F.R.C.S.
Department of Anatomy, London Hospital

Instances of diphallus or double-penis have always excited much interest, partly no doubt because of their infrequency. There are, I believe, no more than 27 cases recorded of its occurrence in man, several cases having been reported more than once.

Since posterior duplicity has recently been the subject of a general and comprehensive article (1) in this *Journal*, and since the theories of its causation, the difficulties of its interpretation and the value of its study as a means of explaining embryological processes were there fully discussed, I shall confine myself simply to a description of the condition in a specimen which has recently come under my observation.

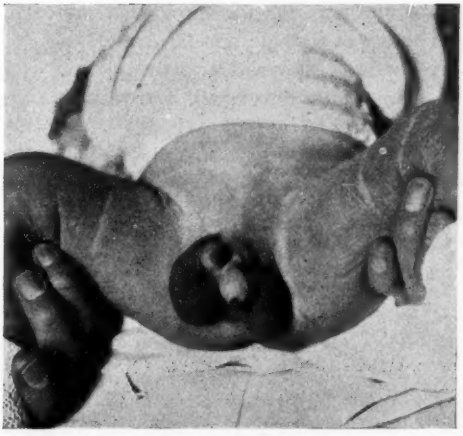

Fig. 1. Photograph of the case during life.

DESCRIPTION OF CASE

A Jewish infant was brought to the London Hospital immediately after birth on account of an imperforate anus. On examination it also exhibited diphallus, and its ultimate death allowed of a dissection of the genitalia, an advantage denied to almost all previous chroniclers of the condition in man.

Each penis was well formed, complete with prepuce and glans, and separate from its fellow in its entire extent. The left was larger and longer than the right and situated a little below as well as to the left. Urine was voided from the left organ; none was observed to pass from the right. The scrotum was cleft in two with a testicle palpable in each half. Advantage was taken of the anaesthesia required for the colostomy, rendered necessary by reason of the atresia ani, to determine the presence or absence of urethrae. A catheter was passed easily through the left organ into the bladder, but could only be passed into a small dimple, representing the external meatus, in the case of the other.

There was no history of any previous abnormalities in the family. The mother was 27 years of age and had one normal child alive and well, aged 6 years.

The infant did not thrive and died a week later. At the post-mortem examination the genito-urinary organs and lower gut were removed entire.

DESCRIPTION OF DISSECTION

In addition to the observations made during life I found the added abnormalities of complete absence of both kidney and ureter on the right side and a very dilated ureter associated with a normal kidney on the left. The bladder was normal save for the absent left ureteral opening. There was a single normal testicle in each half of the scrotum and the prostate was present. The symphysis pubis was fully developed. The rectum fell short of the perineal surface by half an inch.

Dissection of the roots and bodies of the penises confirmed the absence of a urethra on the right side. The right penis resembled a single corpus cavernosum and was attached by a single crus to the right ischiopubic ramus. The crura on the left side were both attached to the left ischiopubic ramus.

Fig. 2. Diagram of the penises with skin removed showing attachment to symphysis.

HISTOLOGICAL EXAMINATION

The section through the left penis was normal showing two corpora cavernosa, one corpus spongiosum and a urethra with numerous peri-urethral (Littré) glands. Each corpus had a well-developed fibro-elastic sheath. Several tributaries of the dorsal vein were seen, but the section did not include the dorsal artery or the common sheath.

The right penis seemed to consist of a single corpus cavernosum provided with an artery and nerves enclosed in a fibro-elastic sheath outside which was some loose connective tissue. In this connective tissue at opposite poles on the circumference were groups of arteries, veins and nerves. In each of these groups there was a touch corpuscle.

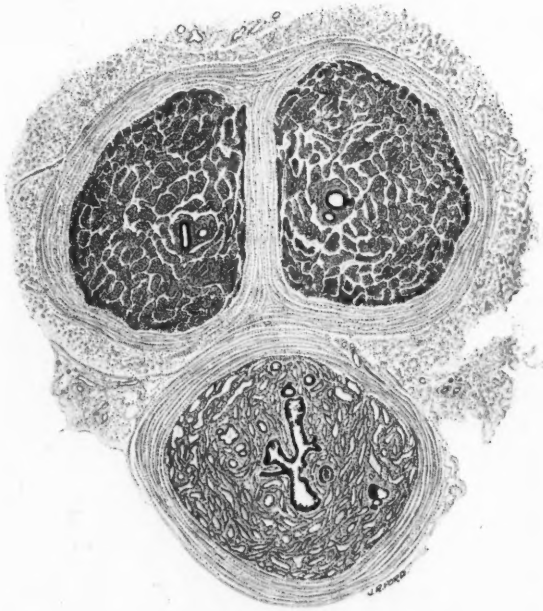

Fig. 3. Cross-section of left penis (× 20).

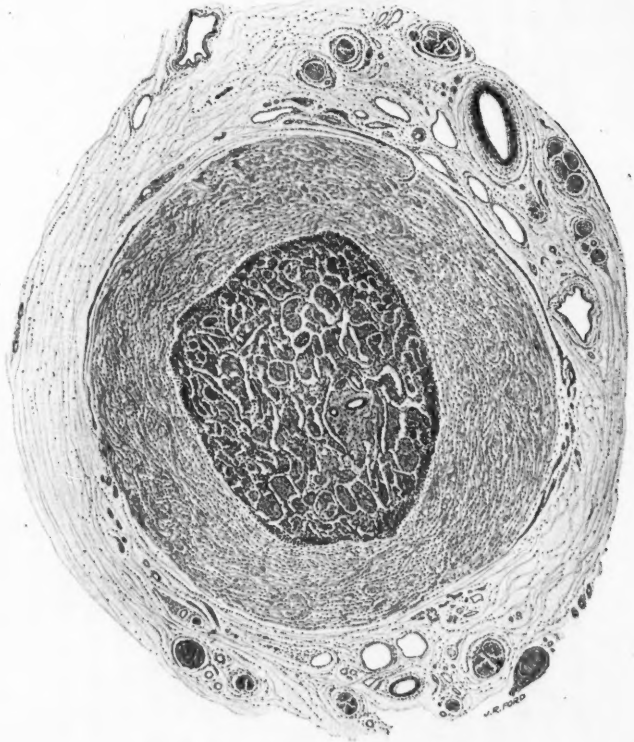

Fig. 4. Cross-section of right penis (× 36).

COMMENTS

The case helps to fill a gap in the knowledge of posterior duplicity, since previous reports of the condition in man have been limited to descriptions of external peculiarities. The abnormalities found correspond, if in less degree, to those shown by non-human specimens. The limitation of the duplicity, in that no extra hind limbs or double pelvis were found, may be interpreted in either of two ways. The genital tubercle may have been the seat of local dichotomy—the teratogenic agent acting upon it while it was in a state of high metabolism—or the teratogenic process has orginally been wider and there has been a partial secondary fusion.

Regarding previous instances recorded in man, the condition has varied from the simplicity of a double glans to two complete members each with a pervious urethra and even a septate bladder. Intermediate gradations between these are the more common. Three have been associated with an extra lower extremity or rather two fused along their length. Six have had atresia ani just as this and in two of these meconium has been passed with the urine demonstrating a persistence of cloacal conditions. The scrotum has been normal or split, the testes normal or atrophic, descended or undescended.

The associated conditions cause a fair mortality in early years, but quite a number of diphallics have reached manhood until the state, hitherto concealed, was discovered by accident. While some of the older observers were prone to endow diphallics with extraordinary sexual powers, the sifted out evidence shows the reverse. Practically all have been sterile. As Ballantyne in *Teratologia* put it: "The apparent anatomical exuberance is usually accompanied by physiological incompetence."

ACKNOWLEDGMENTS

I am indebted to Mr H. S. Souttar, into whose ward the case was admitted, for permission to publish this report, to Dr W. W. Woods of the Pathological Institute, London Hospital, for his kind assistance with the specimen and the histological findings, and to Prof. W. Wright for kind advice.

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CONGENITAL ATRESIA OF THE DUODENUM

By CECIL P. G. WAKELEY, F.R.C.S. Eng., F.R.S. Edin.
Surgeon, King's College Hospital and Belgrave Hospital for Children

Congenital atresia of the duodenum is a well-known condition, and it is necessary that a distinct diagnosis should be made from congenital stenosis of the pylorus. Atresia is more common in the duodenum than in other parts of the small intestine, especially at the entrance of the common bile and pancreatic ducts. The early and accurate diagnosis of the condition which gives rise to symptoms of obstruction of the bowel in a newly born child is of considerable importance, the possibility of relieving the obstruction depending on early diagnosis. In duodenal atresia symptoms of obstruction arise, as a rule, during the first week of life, and vomiting is incessant, while in congenital stenosis of the pylorus symptoms of obstruction appear about the third or fourth week after birth.

The causation of atresia is still unsettled. In 1902 Tandler was able to demonstrate that a proliferation of the epithelial lining of the duodenum takes place in embryos of from 30 to 60 days, and that the lumen thus becomes more or less completely obliterated. In an embryo of 8·5 mm. he found complete obliteration between the outlets of the dorsal pancreas and the common bile-duct. He considered the cause of the occlusion to be the resistance exerted on the expanding epithelium by the surrounding mesenchyme. Since Tandler put forward the theory that the atresia of the duodenum which occurs in the embryo may sometimes persist up to the time of birth, and cause obstruction, Waterson, Gladstone and I have recorded cases where this proliferation of the epithelium has taken place in other parts of the small intestine. Gladstone has suggested that some external condition may contribute to the obliteration of the intestine, such as a fibrous remnant of the right vitelline vein in the lower half of the 8-shaped anastomosis round the duodenum. In a small percentage of cases it is apparently due to fibrous bands, the result of ante-natal peritonitis. The frequency of multiple congenital abnormalities in single individuals appears to indicate that there is a common cause. Previous cases of congenital abnormalities which have come under my notice lead me to believe that the common cause is defective nutrition of the embryo in the early stages of growth, leading to arrest of the normal process of development.

The following is the history of the present case. H. D., a girl, aged four weeks, was brought to the hospital for continuous vomiting which began three weeks after birth. The bowels acted normally, and the child took the breast well. A large sausage-shaped tumour could be palpated in the upper

abdomen. The stomach was very distended. The vomiting was of sudden onset, but not projectile in character.

Gastric lavage was performed, but it did not stop the vomiting. The condition of the baby was very poor; there was a soft systolic murmur over the mid-praecordium, suggestive of a congenital heart lesion. Operation was advised, and a right paramedian laparotomy was performed under local anaesthesia. The stomach was enormous, and was covered by dilated vessels. The first part of the duodenum was also very dilated and enlarged. The

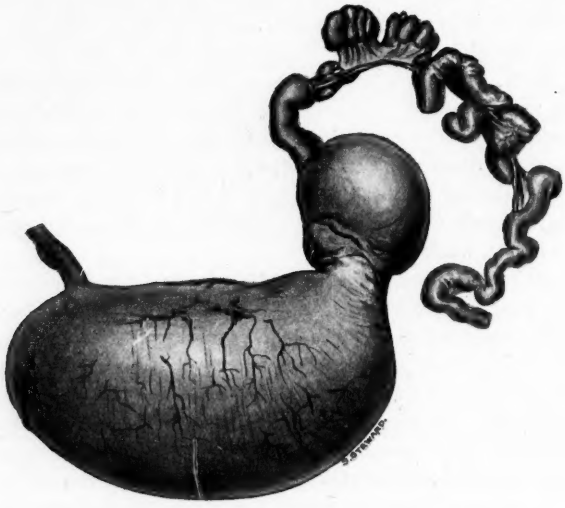

Fig. 1. Specimen of duodenal atresia viewed from behind.

pylorus was not stenosed. There was atresia of the duodenum at the region of the papilla of Vater. The child's condition was so bad that any further operative procedure was deemed inadvisable; the abdomen was therefore closed.

The child died the next day. At necropsy atresia of the second part of the duodenum was found (Fig. 1). There was a large inter-ventricular foramen in the heart, little of the inter-ventricular septum being present. No other congenital abnormalities were discovered.

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OBITUARY NOTICE

THE LATE PRINCIPAL JOHN YULE MACKAY

John Yule Mackay, M.D., LL.D. (Glasgow), Principal of University College, Dundee, and Emeritus Professor of Anatomy, died at Broughty Ferry on 30 March, 1930, in his seventy-first year. He was a son of the Manse, and was born at Inverkeithing, where his father was parish minister before his translation to Blackfriars Church, Glasgow. He received his early education at Glasgow Academy, and in due course passed to the University. During his undergraduate career he distinguished himself in the Classes of Chemistry, Botany and Anatomy, winning class medals in the last two subjects, and gaining the Macfarlane Scholarship.

Obtaining first place in a large class in the Subject of Embryology, he early displayed the promise which in its later development so distinguished his post-graduate work.

In 1881 he graduated M.B., C.M. with commendation, and in 1885 M.D. After graduation he was appointed Assistant to the late Prof. John Cleland, and Lecturer in Embryology in the University of Glasgow.

For twelve years he devoted himself to his duties in Glasgow with singular success. Under the influence of the genius of the late Prof. Cleland he became interested in problems of Morphological Science. In the text-book of *Human Anatomy*—Cleland and Mackay—published in 1896, the sections devoted to the Muscles, Heart and Blood Vessels, Lymphatics and Nerves were the independent contribution of Mackay. He was also joint author with Prof. Cleland in publishing a *Directory for the Dissection of the Human Body*. Along with others he made several contributions in a volume entitled *Memoirs and Memoranda in Anatomy*. An important paper, the "Development of the branchial arterial arches in birds," appeared in the *Philosophical Transactions of the Royal Society of London*, in 1888, and in the same year one dealing with the "Nature and development of the carotid system" was published in the *British Association Report*.

While in Glasgow Dr Mackay took a leading part in the establishment of the Students' Representative Council, and a large share in amassing the fund necessary to start the Students' Union. The experience which he gained then, as a successful intermediary on many occasions between the governing body of the University and the students, no doubt proved helpful to him in later years as Principal.

In 1894 Dr Mackay was elected to the Chair of Anatomy in University College, Dundee, on the resignation of Prof. A. M. Paterson. In 1895 when Principal Peterson resigned his office to accept the Vice-Chancellorship of the

McGill University of Montreal, the Council of University College appointed Prof. Mackay temporarily to the vacancy. He was acting Principal for eighteen months, and in March 1897 his appointment was made permanent. He had a good business capacity which he fully employed in the administrative side. During his tenure of office, five additional Chairs were added, and the number of Junior Staff and students greatly increased.

In Medical Education he played a prominent part, and was Chairman of the Medical Education Committee of the General Medical Council for a number of years.

In 1925 for health reasons he resigned from the duties of the Professorship of Anatomy but continued to act as Principal of the College. As Principal his colleagues remember the courteous and efficient manner in which he presided over their meetings. As Professor he was a fluent, lucid and impressive teacher who possessed the invaluable capability of grasping and carrying with him the interest of his audience.

He was, however, more than an organiser and anatomist, he was a genial man, willing to offer and share pleasures, always ready to help and encourage, and his death has deprived many, not only of a pleasant colleague, but of a faithful and invaluable friend.

D. RUTHERFORD DOW.

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The arteries of the head and neck and the rete mirabile of the Porpoise (*Phocoena communis*), vol. I, p. 61.

Genito-urinary malformation consequent on pelvic deformities, vol. I, p. 33.

Hermaphroditic malformations, vol. I, p. 27.

The arterial system of Vertebrates homologically considered, vol. I, p. 111.

Cases of abnormality of the arteries of the upper limb, vol. I, p. 137.

The relations of the aponeurosis of the transversalis and internal oblique muscles to the deep epigastric artery and to the inguinal canal, vol. I, p. 143.

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REVIEWS

Man's Place among the Mammals. By FREDERIC WOOD JONES, F.R.S. (Edward Arnold, London.) 1929. Pp. 372, Pls. 12, text-figs. 160. Price 21*s.* net.

If there is general agreement among biologists to-day in regard to the main thesis of the evolutionary origin of Man from a more primitive and generalised mammalian ancestor, divergent opinions are held as to the precise route by which the human family has attained to its present status. This uncertainty is inevitable, considering the indirect nature of the evidence from which conclusions may be drawn. Almost half a century ago Bateson wrote that "the attempt to arrange genealogical trees involving hypothetical groups has come to be the subject of some ridicule, perhaps well deserved. But since this is what modern morphological criticism in great measure aims at doing, it cannot be altogether profitless to follow this method to its logical conclusions. That the results of such criticism must be highly speculative, and often liable to grave error, is evident." To-day the construction of genealogical trees is hardly less hazardous than it was fifty years ago, and the problems of phylogeny have become complicated by the accumulation of additional data to a degree which can hardly be appreciated by those who have not made a special study of comparative anatomy to this end. The difficulty of interpreting the evidence is sufficiently indicated by the diversity of conclusions which have been reached by different authorities, and also, in the special problem of human origins, by the personal feelings which have unfortunately often been allowed to give an unscientific bias to arguments. Curiously enough, it is very seldom that phylogenetic speculators take the trouble to enunciate clearly the principles upon which they rely for the interpretation of the data at their disposal, and yet if such speculation is scientifically justifiable, and not mere guesswork, there must be some accepted general principles as its basis. It is impossible here to discuss the relative value of the data available for postulating hypothetical lines of descent and genetic affinities. Suffice to say, whether they are sought in comparative anatomy, palaeontology, or embryology, they require the most detailed and careful consideration from every possible aspect before they may be used as links in a chain of argument, and they provide many pitfalls for the unscientifically minded. One generally accepted principle which is usually relied upon and, indeed, which must be relied upon in the absence of a fairly complete palaeontological record if any conclusions at all are to be made, is that which postulates the irreversibility of evolution. The regaining of primitive characters which have once been lost is probably so rare a phenomenon in evolution, if indeed it ever does occur, that it may be discounted altogether in phylogenetic speculations unless there is the strongest evidence for its presumption. This idea of irreversibility, indeed, is implicit in the arguments of probably every evolutionist. The conception of evolutionary trends with progressive specialisations in various directions, accompanied by loss of evolutionary plasticity, is inherent in all attempts to unravel lines of descent. Multitudes of supposed missing links have been discarded as such after more careful scrutiny because they have been found to possess one or more characters which are regarded as less primitive than the corresponding characters of the form to which they were at one time imagined to have given rise. But what if this principle of irreversibility of evolution be carried to its logical conclusion? This is, broadly speaking, the aim of Prof. Wood Jones in his

latest book, and to our mind it is well that the position with regard to Man's evolutionary status should be examined in the light of this principle by an anatomist who is conversant with all the available details of Primate anatomy. Wood Jones' thesis is one which can be logically argued on the basis of this principle even though his conclusions may be inacceptable to the generality of anatomists or, indeed, may ultimately prove to be erroneous. If irreversibility of evolution is so generally implied by evolutionists, it is necessary that it should be explicitly affirmed and applied in detail to the evolution of Man. If the conclusions which result therefrom are untenable, then some revision is needed in regard to a common conception of evolutionists on the question of evolutionary specialisation and its accompanying loss of plasticity.

Unfortunately, Wood Jones rather tends to prejudice the reader against a fair and calm enquiry into the tenability of his conclusions by some unhappy attacks on authorities of recognised standing, and by including in his arguments data the accuracy of which is open to question or, in some cases, which are definitely erroneous. The reviewer, however, wishes deliberately to ignore these defects which, in themselves, do not affect the main lines of argument.

Wood Jones lays considerable stress on the prevalence of the phenomenon of convergence or parallelism in evolution, and, indeed, this is a necessary corollary of the thesis of irreversibility. The reviewer is in sympathy with him on this point. If evolution is an orderly and progressive process, working on material which ultimately is derived from the same source and endowed with the same potentialities, and if this material is subjected to similar environmental influences, it is to be anticipated that similar forms and characters may independently appear during the course of evolutionary development. As a matter of fact, it seems probable that parallel evolution has occurred to a vastly greater degree than most anatomists even now realise. There is no *a priori* reason why this should not be so. The remarkable resemblance between the brain of a gorilla and that of Man may be interpreted as the result of a common origin from a form in which the brain was at least as highly developed as that of the giant ape. It may be so. But a definite assertion on this point could only be made if it is first demonstrated that the brains of these two primates owe their development to a combination of fortuitous circumstances such as would not be likely to have occurred more than once in evolutionary history. If Dudley Morton is correct in the conclusions he draws from an intimate study of the feet of Primates, that the human stock could only have been derived from an ape-like progenitor no larger than the modern gibbon, then, indeed, there is *prima facie* evidence that the gorilla actually did acquire the peculiarly human characteristics of its brain independently of Man.

Arguing on such lines as these, Wood Jones would maintain that there can be no question of Man being derived from a "gorilloid" ancestor. Further, since the anthropoid apes, as a group, exhibit certain specialisations in limbs, cranial characters, teeth, etc., which are not found in Man, he argues that Man has not been derived from any ancestral form which can be strictly called an anthropoid ape. This is a legitimate argument in so far as reliance can be placed upon the general thesis of irreversibility in evolution, and in so far as certain features of modern anthropoid apes, such as elongated forelimbs, a tendency to degenerate changes in the thumb, certain osteological features of the foot, etc., may be regarded as essential elements in the make-up of what we call an "anthropoid ape." If it is inferred that the human stock must have branched off from the common Man-ape stock at a time when the members of this common stock were no larger than the modern gibbon, when the fore-limb and hind-limb proportions still retained their primitive condition, and before certain anthropoid ape specialisations had put in an appearance, then Man cannot be accurately said to have been evolved from an anthropoid ape, unless, indeed, the term "anthropoid ape" be defined as having a wider application than it is customarily accorded. As a matter of fact, a great deal of the current controversy

regarding the evolutionary origin of Man arises from the too frequent use of a vague and undefined nomenclature. Such terms as "gorilloid," "anthropoid," "pithecoid," "tarsioid," are examples of such a nomenclature. "Gorilloid" can only be interpreted as an adjectival form of the word "gorilla," and a gorilloid animal, therefore, can only be a giant anthropoid with specialised features of the limbs, skull, teeth, etc., such as could hardly have been present in an ancestral form of the Hominidae. To speak, therefore, of Man's "gorilloid heritage" is clearly misleading. "Anthropoid" is a term which is even more abused. Anthropologists quite commonly use it to mean "ape-like," the very reverse of its correct meaning, and to talk of the anthropoid ancestry of Man is likely to lead to many fruitless controversies unless the term is adequately defined. With regard to monkeys, again, Wood Jones is no doubt technically justified in his conclusion that "the whole stock of the Old World Monkeys is excluded from any share in human ancestry," if it is admitted, for instance, that bilophodont molars are essential elements in the make-up of what we call an Old World Monkey, and that they constitute a specialised character such as could not have given rise to the human type of molar. But if so much is conceded, it is equally legitimate to argue, on similar grounds, that the whole stock of Old World Monkeys is excluded from any share in the ancestry of the anthropoid apes. Here Wood Jones shows a certain inconsistency, for he appears to regard the anthropoid apes as little more than overgrown Catarrhines. Now it will be apparent that this discussion of the relation of the human stem to the monkey stem largely involves the question of terminology and definition. There can be no doubt, of course, that somewhere in Man's ancestry there existed a form which must have been remarkably like the animals we call Old World Monkeys, and which certainly would be called a "monkey" by most people. But Wood Jones would maintain that it could not have been a member of the Old World Monkey stock, in the strict sense of the term, precisely because it would not yet have acquired certain specialised characters which are found in this group as this group is commonly defined. Therefore, he says, the popular idea that Man is descended from a "monkey" is misleading, and he believes that anthropologists have not made this point sufficiently clear in their more popular expositions.

While Wood Jones is right to draw attention to the careless use of terminology, he himself errs in a similar direction by his use of the term "tarsioid." He believes that the human stock separated from the rest of the Primate stock at a period when the latter had not passed beyond the tarsioid level of evolution. But what is the "tarsioid" level precisely? The term "tarsioid," unless it is expressly defined otherwise, can only mean an animal similar to the members of the suborder Tarsioidea as that suborder is properly defined, that is to say, possessing peculiar eyes, specialised hind-limbs, etc., which no one supposes to have existed in any ancestor of Man. No doubt Man has ultimately been derived from a form which exhibited many of the primitive features found in the known Tarsioids, but this does not mean that any ancestor of Man can be accurately termed a Tarsioid. A Tarsioid stripped of its specialised characters would cease to be a Tarsioid.

Whatever may be the real facts of the case, Wood Jones' thesis that the human stock may have separated from the rest of the Primate stock in a pre-simian stage of evolution is one that can be legitimately argued, and to which serious consideration should be given.

Wood Jones' opinion regarding the inclusion of the Lemurs among the Primates is well known. He believes that the common ancestor of the Tarsioidea and the Lemuroidea must have been so remarkably primitive that it could hardly be designated a Primate. He proposes, partly on these grounds, to separate entirely the Lemuroidea (which he includes with the Tupaiidae in a group called Strepsirhini) from the group containing the Tarsioidea and Anthropoidea which he calls Haplorhini. This, again, is a point of view which may be reasonably argued even though the opinion of anatomists will be heavily against its acceptance. It is certain that a

common ancestor of the Tarsioidea and Lemuroidea could not have been a "lemuroid," as lemuroids are properly defined. Indeed, Elliot Smith has already recognised this, for, in a tentative scheme, he derives the Tarsiers and Lemurs from a common group which he calls "Prosimiae primitivae." To talk, therefore, of the lemuroid ancestry of Man is not permissible. The question as to whether or not Lemurs may be suitably called Primates will depend on whether the hypothetical "Prosimiae primitivae" are forms which can legitimately be called Primates, as Primates are properly defined.

This review sufficiently indicates the controversial nature of the subjects dealt with in Wood Jones' book. The attractive and refreshing style in which it is written makes it remarkably stimulating to read, and the numerous text-figures and plates considerably enhance its interest. Apart from these considerations, we are grateful to Prof. Wood Jones because his book does emphasize the urgent need for a careful revision of the nomenclature which is so commonly employed by evolutionists who occupy themselves with the problems of Man's origin. This problem, by the very nature of the evidence at present available, must be a vexed one, but the controversies to which it gives rise will be vastly more profitable when the nomenclature is based on terms which are accurately defined.

Vertebrate Zoology. An Introduction to the comparative anatomy, embryology and evolution of Chordate animals. By G. R. DE BEER, with an Introduction by JULIAN S. HUXLEY. Sidgwick and Jackson, Ltd., Text-Books of Animal Biology. Pp. xx + 505, with 185 illustrations. London, 1928. 15*s.* net.

The majority of text-books of recognised merit dealing with the Morphology of Vertebrate animals belong to that school which demands that morphology alone shall form the basis and core of zoological teaching. This is the old school which dates from the time when "animal morphology" and "zoology" were equivalent and synonymous terms. The growth and evident importance of the newer branches of zoology, such as comparative physiology, genetics, *Entwicklungsmechanik*, ecology, etc., soon demanded that they also should be taken into account in teaching zoology. Such demand was met by linking them on as accessories to the central morphological theme. This was the natural method, and the best so long as these new branches of study were in an embryonic state. That, however, is no longer the case. Many of these new branches of zoology have assumed the status of subjects co-equal in importance with morphology. They demand a fair share of attention and an equal place in the zoological curriculum. This requirement is being met by suitable adjustment of the syllabus in many zoological schools to-day. A need has arisen, in consequence, for books adopted to this new mode of teaching which the present series of "Text-books of Animal Biology" aims at supplying.

The place which morphology must take in the new scheme of things is outlined in a clear and convincing manner in the introduction to this book. It provides the best educational discipline for zoology and should remain in a central position in the curriculum provided that it does not arrogate to itself an unfair share of the students' time. Moreover, its points of contact

with the other important branches of zoology must be emphasised. These requirements Mr de Beer has attempted to fulfil, with considerable success. His book is an admirable exposition of Vertebrate morphology, from this point of view, and is suited to the requirements of senior students. It is remarkably full and complete for its size and will prove, perhaps, of even more use to the teacher than to the student. It is divided into five parts, of which the first two deal respectively with the anatomy and embryology of suitable types. The third part is comparative and serves to link up these various types with each other and to introduce significant facts concerning other animals. The fourth part deals with the evolutionary morphology of the Vertebrates, while a short conclusion constitutes the fifth part.

The numerous illustrations, many of which are new, are in line. Their value is enhanced by the fact that the majority are suitable for black-board drawings. A few are too diagrammatic, whilst others might, perhaps, be improved by more careful drawing. The majority, are, however, excellent.

The editor and publishers are to be congratulated on having secured this book for their series. The author will, undoubtedly, have the satisfaction of seeing it take its place among the standard English text-books of Zoology. The companion volume, now in preparation, on Invertebrate Zoology, will be awaited with interest.

A Text-Book on the Artistic Anatomy of the Human Form. By U. W. A. Parkes. (London: John Bale, Sons and Danielsson, Ltd.) 1923. Limp cloth 7*s.* 6*d.*, cloth boards 10*s.*

The text of this book provides a simple account of the skeleton followed by a description of the muscles and fasciae influencing external body form. The surface markings caused by bones and muscles in the living, moving body are fully emphasised. Illustrations, a large number drawn from specimens in the R.C.S. Museum, occupy rather more space than the text. Diagrams of bones and muscles can be contrasted with "action sketches" of surface form. The text, while simply written for lay readers, seems to be anatomically correct, and with the copious illustrations should adequately fulfil the expressed purpose of providing a book of study and reference for art students. On pp. 99 and 101 the adductor longus is wrongly labelled "adductor brevis." The hands and feet—so often weak parts of life studies—might usefully have received fuller consideration.

Introduction to the Study of the Nervous System. By E. E. Hewer and G. M. Sandes. (William Heinemann, Ltd.) 21*s.* net.

From the fact that this book is limited to 98 pages of letter press, it will be realised that the subject has been dealt with in the briefest possible manner. There are also included 55 diagrams, mostly in colour, illustrating the course

of the main fibre tracts of the central nervous system. There are statements which are questionable and others which are wrong. We refer to such statements as that the thalamocortical fibres to the postcentral gyrus are limited to the anterior limb of the internal capsule, that the spinotectal tract passes to the inferior corpus quadrigeminum and is there relayed on to the post-Rolandic cortex, that the pyramidal tract rises in the ascending parietal convolution (p. 13), that the tertiary olfactory neurones pass to the epithalamus and the ganglion habenulae (*sic.*) by the stria terminalis, that the olfactory tract fibres to the piriform cortex are interrupted in the tuberculum olfactorium (Diagram 15), that gustatory impulses are relayed from the nucleus of the fasciculus solitarius up in the medial fillet and through the thalamus to the post-Rolandic cortex (Diagram 25), that the ganglion habenulae is connected with the hippocampal gyrus, that the globus pallidus represents the oldest motor cortex, etc. These are but a few of the statements open to criticism.

Handbuch der Anatomie des Kindes. Zweiter Band, 2. Lieferung. Sinnesorgane des Kindes. By PETER, WETZEL and HEIDERICH. (Munich: Bergmann.) 1929. Pp. 155–303. Figs. 64–167. Price 28 M.

This section of the second volume of the *Handbuch der Anatomie des Kindes* maintains the high standard set by the previous parts. The apparatus of hearing is described by Lange of Leipzig and the age changes both as regards the dimensions and pneumatisation are excellently figured. The histology and pathology are discussed adequately. The section dealing with the Nose, by Karl Peter of Griefswald, provides a most valuable set of tables of the dimensions of the various sinuses at successive ages. The histology of the tissues is described in such a way as to form a sound basis for the morbid anatomy of the region.

The Skin, by Joseph Becker of Bonn, is a compact presentation of our knowledge of the development of the skin, of the condition in the new-born, and of the development of the hair, vessels, pigment, nerves and glands. The anatomical aspects of the problems afforded by the recent work on the vascular reactions of the skin could hardly have been incorporated, but such information is urgently required by many workers to-day. The age changes as regards hair, pigment and glands are tabulated in convenient form.

Prof. Dragendorff of Griefswald has succeeded in amassing the details of measurements of size, content and mural thickness of the chambers of the heart which are scattered throughout the literature. The dimensions of the papillary muscles and valves are also included. The development of the heart, the changes in the neo-natal period and the structures of morbid significance are well depicted.

This work is an invaluable time-saver to the laboratory worker and the clinician. Anatomical in its outlook it is provocative to the physiologist and a companion volume on the physiology of the child would be welcomed.

Ballière's Synthetic Anatomy. **By J. E. Cheesman. Part V, The Leg. Text pp. 6. 12 Plates. Part VI, The Foot. Text pp. 6. 12 Plates. (London: Ballière, Tindall and Cox.) 1929. Price 3*s.* net per part.**

The general features of this Atlas of Anatomy are now well known, and earlier parts in the series have been reviewed already in the *Journal of Anatomy* (vol. LXI, p. 386). One of the present sections deals with the Leg from the popliteal space downwards on a scale about one-third natural size, while the other illustrates the Foot in fuller detail, almost life size. The ingenious designs of the author have been executed by the publishers in praiseworthy fashion, the complicated colour registering required only missing perfection in some of the finer details in the sole of the foot. The Atlas should prove useful to students in revising and consolidating their topographical knowledge after dissecting the parts, and offers unique assistance in learning surface anatomy. It will be specially useful to those who find difficulty in visualising anatomical relationships. To make full use of the plates genuine application is required, but time so spent will yield a knowledge of the structures themselves much superior to the parrot information obtained from a cram book. Teachers deficient in natural aptitude for "blackboard reconstruction" will find helpful suggestions in this carefully thought-out presentation of structures in successive planes.

The Autonomic Nervous System. **By Albert Kuntz, Ph.D., M.D. (Baillière, Tindall & Cox, London.) 1929. Pp. 576. Price 31*s.* 6*d.* net.**

Many text-books, even recent ones, give an account of the autonomic nervous system which is not in accordance with modern ideas, so that those wishing to familiarise themselves with recent developments have been compelled to consult numerous papers and monographs.

To all such this book will be welcome; and Prof. Kuntz, himself a prominent worker on the subject, has given us an excellent and well-correlated account of the investigations which have been made by himself and others.

Due credit is given by the author to the physiologists of the Cambridge school who did so much of the pioneer work, and whose results have formed a basis for the large amount of morphological and experimental work carried out in the United States and elsewhere.

The book is an excellent example of the advantage of including under one cover anatomical, physiological, and clinical data; and although we are still far from a clear understanding of this important division of the nervous system, Prof. Kuntz can claim to have infused some life into the dry anatomical details.

As in other parts of the nervous system, morphological and clinical studies seldom keep pace with one another and it is often difficult to correlate clinical observations with either. The author may be complimented on the fact that he has avoided the invocation of hypothetical nerve pathways to explain certain phenomena in visceral pathology.

With regard to the vexed question of the developmental origin of the autonomic neurones, a fair statement of the position is given, and the suggestion provisionally adopted that many, if not all, of the cells which migrate into the system from the neural crest give rise to neurolemma cells.

The tonus question is discussed and the conclusion reached that tonus may be influenced by the autonomic system either directly, or indirectly, through the vascular system. "Much of the autonomic nervous influence on skeletal muscle is expressed through its influence on muscle metabolism." It is pointed out that experiments involving decerebrate rigidity are not well adapted to reveal the influence of sympathetic innervation on tonus. The relation of the autonomic nervous system to such conditions as angina pectoris and megalocolon is discussed in an unbiased and scientific manner, which makes the book a pleasure to read.

It is made clear that there is no rational anatomical or physiological basis for the operation of periarterial sympathectomy, but that this does not preclude its value in selected cases.

The book is well got up, the illustrations being clear and well selected, and there is a good bibliography.

The Internal Secretions of the Ovary. By A. S. Parkes. Monographs on Physiology. (Longmans, Green and Co., Ltd., London.) 1929. Pp. xv + 242. 69 Figs. Price 21*s.*

This praiseworthy addition to the distinguished monographs on Physiology is a valuable presentation of the main paths of research in relation to the ovary, and affords a valuable bibliography for the laboratory worker. The chapters dealing with sex periodicity and the various types of oestrous cycle are excellent. The oestrous cycles of laboratory animals are now so well known that it is surprising how little progress has been made by clinical gynaecologists in correlating the processes in Man and the Primates with those in laboratory animals, and the author indirectly indicates the need for research in this field.

Three internal secretions of the ovary are described, one controlling sexual characters, one controlling oestrus and one controlling the changes in the female organs during pregnancy. The preparation of active extracts of the first two has been accomplished and Dr Parkes made an important contribution to the subject when he proved that oestrin was formed in the early corpus luteum or ripe liquor folliculi rather than in the late solid corpora lutea. His quantitative estimation of the distribution of oestrin in the body fluids during pregnancy and of its rapid disappearance after parturition is a valuable example of the newer laboratory methods. Parkes maintains as a result of his experiments, including sterilisation by X-rays, that the Graafian follicle is not the essential source of oestrin, that the periodicity of oestrus is not governed by periodic maturation of the follicles and that elimination of the corpora lutea of ovulation has no effect on the periodicity of oestrus.

The recent work of Smith and Engle on the anterior lobe of the pituitary gland is described in detail and the probable effect of the gland on the ovary and oestrous cycle is considered. The newer methods of assay of the potency of the extract of the anterior lobe are presented. The relationship of the corpus luteum to the mammary gland and the rôle of oestrin in parturition is linked up with the function of the oxytoxic principle of the posterior lobe of the pituitary gland.

A more detailed description of the minute anatomy of the ovary and a clearer definition of what constitutes "interstitial tissue" may be looked for in the future editions of a book which bids fair to become a standard work of reference.

Rickets, including Osteomalacia and Tetany. By ALFRED F. HESS. (Henry Kimpton, London.) 1930. Pp. ix + 485. 52 Figs. Price 25*s.* net.

The distinguished clinical Professor of Pediatrics in New York has had the good fortune to belong to the band of pioneers in several movements in modern medicine. In no direction has any physician and laboratory worker accomplished more than Prof. Hess has in relation to the "Newer Rickets" from 1918 to the present day. The book is written for the general practitioner, the nutrition worker and the student of bone growth in health and disease. No text-book of recent years indicates more clearly the manner in which the clinician and biochemist have attacked problems which should have been of prior interest to the anatomist and histologist. The time-worn conception of bone as a fixed and inert tissue has been destroyed by the clinician and the radiographer.

The contrast between the history of clinical rickets and the history of experimental rickets in animals is so admirably delineated that no unbiased person dare decry the value of the experimental method. The progress in our knowledge of the aetiology of rickets dates almost entirely from 1918, and it is surprising that radiographical features as an aid to diagnosis were not appreciated until 1916. Hess presents a valuable account of the history, distribution and aetiology of rickets. The theories of calcification suffer somewhat in that he, like Mellanby, fails to distinguish between the problem of calcification in cartilage and true bone formation. The studies on metabolism, pathology and symptomatology of rickets are followed by valuable chapters on the radiographic signs and differential diagnosis. Juvenile rickets and osteomalacia are described in such a manner as to bring them, with rickets, as far as possible into a single group. The chapter on tetany affords the best description that we have of the complexity of the condition and illustrates how the experimental method has led to satisfactory prophylactic treatment in supersession to the older and somewhat unsatisfactory symptomatic treatment.

In regard to treatment, Hess is whole-heartedly with Pliny in believing that "Sol maximum remediorum est." The history of the stages which lead to the production of irradiated ergosterol is one of the romances of medicine and Hess is to be congratulated both on the part which he has played therein, his appreciation of the work of others, his strong plea for public health measures and his guarded references to much in the way of the "newer window panes." Hess prefers ultra-violet therapy and irradiated ergosterol to cod liver oil therapy and is especially cautious as to the significance of vitamin A which occurs with the anti-rachitic vitamin D in the natural oil. He is also careful to distinguish between the proved rôle of vitamin D in rickets and the possible rôle of vitamin D in dental caries.

Comparative Neurology. By JAMES W. PAPEZ. (Thomas Crowell Co., New York.) 1929. Pp. 544. 315 Figs. Price 6$.

There is no better introductory laboratory course on the form, function and structural interpretation of the nervous system than this valuable book by Prof. Papez of Cornell University. The first part of the book is devoted to the comparative topographical anatomy of the brain of mammals, and the author is particularly brief and clear in his descriptions. The second part of the book deals with the microscopic structure of the mammalian nervous system, and covers the territory from the peripheral nerves to the spinal cord, hind-brain, mid-brain and cortex. The third part deals with the comparative anatomy of the fibre tracts and functional centres in type brains, ranging from Reptiles, Birds, Amphibians, Fishes, Cyclostomes to *Amphioxus*.

The simple presentation of the facts of comparative anatomy, together with the brief indications of function, maintain the interest of the student throughout. The structure of the olfactory brain includes an adequate account of the theory of the function of the hippocampus. The neopallium is described in terms of the work of Flechsig, Brodmann, Elliot Smith and Campbell, and the more recent work of Economo and Koskinas on cortical lamination is included. The physiology of the cerebral cortex from the time of Fritsch and Hitzig to the more recent work of Pavlov is discussed, the sole notable omission being Head's work on aphasia.

The author is to be congratulated on producing a manual of Comparative Anatomy which focusses attention on the dynamic character of the evolutionary processes in the brain, and on the gradual emergence into increasing significance of the fore-brain. Not least among the special characters of the book is the straightforward presentation of that development of the cortical pattern in the primitive mammalian brain which has been so strongly emphasised by Elliot Smith. As to terminology, certain objections may be raised to such terms as "somatic" pallium. Yet the book is a noteworthy success.

Heredity in Man. By R. Ruggles Gates. (Messrs Constable, London.) 1929. Pp. xiii + 385. 87 Figs. Price 24*s.* net.

This book, an expansion of the previous one, *Heredity and Eugenics*, by the distinguished Professor of Botany at King's College, University of London, is at one and the same time a proof of Prof. Gates's broad interest in biology, and a serious criticism of present-day anatomists in that so essential a need has been supplied by a devotee of plant life. The subject of heredity and variation does not loom so large in the medical horizon as it did in the days of Galton and Bateson, yet the rediscovery of Mendel's work on the one hand, and the patient work of Karl Pearson and his co-workers on the other, have done much to stimulate the more careful recording of inherited abnormalities and diseases by the younger generation of medical men.

Prof. Gates proceeds from a simple introduction dealing with the general aspects of heredity to the inheritance of stature, and the problems of bodily habitus. Hereditary abnormalities of the eyes, eye colour, hair colour and albinism lead to a consideration of special skin diseases. The chapter on blood grouping in the various races is up to date and the section dealing with blood dyscrasias, metabolic diseases and allergic conditions is most instructive. The various skeletal abnormalities of the hands and feet, harelip, deaf-mutism and other conditions met with in any hospital clinic are described in considerable detail.

The chapter on racial crossing provides a sober and reasoned presentation of the utmost importance to the politician and Empire-builder who stays at home. The author holds that the intermixture of unrelated races is eugenically undesirable and strongly disapproves of the dilution and degradation of the more advanced race by admixture with a race presenting primitive mental characters.

A subsequent edition will no doubt incorporate the recent work of Castle and Gregory who have shown that differences in racial size in large and small rabbits are due to differential rates of cell division in the respective zygotes of large race and small race ancestry. This indicates that the endocrine factor is not the sole factor. Furthermore the recent work of Bagg has shown that the earliest lesions in the descendants of X-rayed mice, in which abnormalities and defects of the limb are common, consist of haemorrhagic blebs on the limb buds in the earliest stages of development. This experimental observation throws considerable light not only on the genesis of deformities of the limbs, but also serves as a link with the well-established group of cases presenting naevoid conditions of the meninges in combination with varying degrees of amentia.

We look forward to the day when an anatomist will produce a book of such service to the student of plant life.

INDEX

Adrenals, early, Some notes on. By Dr M. S. Honan, 194

Anatomical routes by which infection may pass from the Nasal Cavities to the Brain. By Prof. Le Gros Clark, 121

Anatomy. Comité International des recherches des parties molles (Parties non osseuses). By Sir Arthur Keith, 99

Animals, Fossil, Brain of—a review. By Ariëns Kappers, 254

Anthony, R. et J. De Grzybowski. Le *neopallium* des équidés. Étude du développement de ses plissements, 147

Aortic Arch, Complete double. By Robert D. Lockhart, Ch.M., 189

— right. True congenital diverticulum of the Trachea in a subject showing also right Aortic Arch. By E. P. Stibbe, 62

Appendix, A diverticulum of the. By Thomas Walmsley, M.D., 47

Appleton, Dr A. B. An example of the M. cervico-costo-humeralis, 109. For original communication see vol. LXIII, 434

Arteries, Thyroid, considered in relation to their surgical importance. By Lambert Rogers, M.Sc., F.R.C.S., F.A.C.S., 50

Artery, Bronchial, left, abnormal. Anatomical Note. By R. W. Hewitt, 363

— Internal Mammary, lateral thoracic branch of. By Dr E. P. Stibbe, 127

Ashley-Montagu, M. F. Note on a rare type of Pterion in the Gorilla, 247

Atlas and Axis Vertebrae, fusion of. By A. J. E. Cave, M.B., 337

Atresia, Congenital, of the Duodenum. By Cecil P. G. Wakeley, F.R.C.S. (Eng)., F.R.S. (Edin.), 527

— Follicular, the Ovary of *Ornithorhynchus*, with special reference to. By Mary Lee Garde, B.Sc., 422

Axis Vertebra with absent costal element (cervical rib). By A. J. E. Cave, M.B., 116

Babe aged two months, Cystic Ovary in. By H. A. Harris, D.Sc., M.B., B.S., 303

Bantu Native of South Africa, Report on a specimen of fused pelvic kidney found in. By L. R. Shore, M.A., M.B., M.R.C.P., D.P.H., 344

— — series of skeletons of, Abnormalities of the Vertebral Column in. By L. R. Shore, M.A., M.B., M.R.C.P., D.P.H., 206

Beattie, Dr J. The higher sympathetic centres in the Diencephalon, 124

de Beer, G. R. Vertebrate Zoology. An Introduction to the Comparative Anatomy, Embryology and Evolution of Chordate Animals. With an introduction by Julian S. Huxley. Review, 534

Begg, R. Campbell, M.C., M.A., M.S., M.D., Ch.B., F.R.C.S. (Edin.), M.R.C.S. (Eng.), L.R.C.P. (Lond.), F.A.C.S., F.C.S.A. The Urachus: its anatomy, histology and development, 170

Bird utterances, Technique of. By Prof. C. J. Patten, 108

Bird's heart, conducting system of the. By Francis Davies, M.D. (Lond.). Further studies, 129, 319

Blair, Prof. D. M. The presence of deep Submaxillary Lymph Glands in the substance of the Submaxillary Salivary Gland, 111

Blastocyst of Cavia, Observations on the structure and mode of Implantation. By Prof. J. P. Hill and Dr G. S. Sansom, 113

Bone, Vascular supply of, with special reference to the Epiphysical Cartilage. By H. A. Harris, M.B., B.S., D.Sc., 3, 123

Bones, Long, growth of in Foetal Life, as exemplified by a case of Foetal Syphilis. By H. A. Harris, M.B., B.S., D.Sc., 1

— — Radiological investigation of the Epiphyses. By R. S. Paterson, M.D., D.M.R.E., 28

Brain of Fossil Animals—a review. By Ariëns Kappers, 254

Bramdell, Dr F. W. Histology of the Gonads of an Hermaphrodite Pig, 111

Bronchial Artery, left, abnormal. Anatomical Note. By R. W. Hewitt, 363

Bursal Sac in the substance of the Subscapularis. Anatomical Notes. By E. P. Stibbe, 98

Cameron, John, M.D., D.Sc. Craniometric Memoirs. No. II. The human and comparative anatomy of Cameron's Cranio-Facial Axis, 324

Cameron's Cranio-Facial Axis, human and comparative anatomy of. By John Cameron, M.D., D.Sc., 324

Cartilages of Santorini, Function of. By V. E. Negus, 111

Cave, A. J. E., M.B. An Axis Vertebra with absent costal element (cervical rib), 116

— Anomalies of sixth Cervical Vertebra in Man, Orang and *Macacus*, 118

— Fusion of third and fourth Cervical Vertebrae, 118

— On fusion of the Atlas and Axis Vertebrae, 337

— Skull showing a cranio-pharyngeal canal and asymmetrical maxillary sinuses, 126

Cavia, Blastocyst of, Observations on the structure and mode of Implantation. By Prof. J. P. Hill and Dr G. S. Sansom, 113

Cavum septum pellucidi, abnormal. By Prof. Green, 128

Cerebral and Cerebellar Veins, functional significance of the arrangement of. By John S. B. Stopford, F.R.S., 257
Cervical Rib. An Axis Vertebra with absent costal element (cervical rib). By A. J. E. Cave, M.B., 116
Cervical Sympathetic and the descendens cervicalis, Communicating branches between. By Alvaro Rodrigues, 308
Cheesman, J. E. Ballière's Synthetic Anatomy. Part v, The Leg. Part vi, The Foot. Review, 537
Circulation, Mesenteric, Observations on. By A. J. Cokkinis, M.B., B.S. (Lond.), F.R.C.S. (Eng.), 200
Clark, Prof. W. E. Le Gros. Anatomical routes by which infection may pass from the Nasal Cavities to the Brain, 121
— Method of demonstrating Lymphatic plexuses, 115
— The Anterior Nuclei of the Thalamus in Insectivores, 125
— The Thalamus of *Tarsius*, 371
Coghill, G. E. Anatomy and the problem of Behaviour. Lectures delivered at University College, London, 1929. Review, 104
Cokkinis, A. J., M.B., B.S. (Lond.), F.R.C.S. (Eng.). Observations on the Mesenteric Circulation, 200
Congenital Atresia of the Duodenum. By Cecil P. G. Wakeley, F.R.C.S. (Eng.), F.R.S. (Edin.), 527
Cooper, Eugenia R. A., M.D., M.Sc. The Histology of the retained Testis in the human subject at different ages, and its comparison with the Scrotal Testis, 5
Cortex, Suprarenal, observations on the growth of. By W. C. Osman Hill, M.D., Ch.B. (Birm.), 479
Cortical representation of the Macula. By G. Elliot Smith, F.R.S., 477
Craniometric Memoirs. No. II. The human and comparative anatomy of Cameron's Cranio-Facial Axis. By John Cameron, M.D., D.Sc., 324
Cutaneous Glands of Man. By H. H. Woollard, 415
Cyst, bursal, in subscapularis (?). By Dr E. P. Stibbe and Dr F. Davies, 119

Darnley, Lord. The Diploic Veins as evidence of age, with especial reference to the skull attributed to Lord Darnley. By Dr H. A. Harris, 115
Davies, F., M.D. (Lond.). The conducting system of the Bird's heart, 129; Further studies, 319
Davies, Dr F., and Dr E. P. Stibbe. Complete absence of the quadratus femoris muscle, 119
— — Bursal cyst in subscapularis (?), 119
Diencephalon, Higher sympathetic centres in. By Dr J. Beattie, 124
Diphallus, human, case of. By Charles Donald, F.R.C.S., 523
Diploic Veins as evidence of age, with especial reference to the skull attributed to Lord Darnley. By Dr H. A. Harris, 115
Diverticulum, Congenital, of the Trachea in a subject showing also right Aortic Arch. By E. P. Stibbe, 62
— of the Appendix. By Thomas Walmsley, M.D., 47
Donald, Charles, F.R.C.S. A Case of human Diphallus, 523
Dow, D. Rutherford. Obituary notice of the late Principal John Yule Mackay, 529
Duodenum, Abnormal. By Capt. B. S. Nat, M.B., Ch.B., F.R.C.S., I.M.S. and P. D. Mookerji, I.M.S., 250
— Congenital Atresia of. By Cecil P. G. Wakeley, F.R.C.S. (Eng.), F.R.S. (Edin.), 527

Edgeworth, F. H., M.D. On the masticatory and hyoid muscles of larvae of *Xenopus Laevis*, 184
Edwards, Harold, M.S., F.R.C.S. Aberrant accessory Ureter associated with Hydronephrosis, 94
Egg Tooth of *Ornithorhynchus*, description of, together with some notes on the development of the Palatine processes of the Iremaxillae. By H. L. Green, 512
Embryos, Human, young, formation of the connecting stalk and the extension of the Amniotic Cavity towards the tissue of the connecting stalk in. By J. Florian, M.D., 454
Epiphyses of the Long Bones, Radiological investigation of. By R. S. Paterson, M.D., D.M.R.E., 28
Epiphysial Cartilage, and the Vascular supply of Bone. By H. A. Harris, M.B., B.S., D.Sc., 3, 123
Eye, Motor Nerves of, Sensory components of. By E. P. Stibbe, 112

Fallopian tube and Uterus, case of undescended testicle associated with. By R. Rutherford, 121
Fawcett, Prof., M.D., F.R.S. A model of the Left Half of the Human Mandible at the 17 mm. C.R. Stage, 369
Ferret, early development of: The Pronuclei. By Donald Mainland, M.B., Ch.B. (Edin.), 262
Flexor pollicis longus, Two unusual abnormalities of. By Prof. C. M. West, 126
Florian, J., M.D. The formation of the connecting stalk and the extension of the Amniotic Cavity towards the tissue of the connecting stalk in young Human Embryos, 454
Foetal Life, growth of Long Bones in, as exemplified by a case of Foetal Syphilis. By H. A. Harris, M.B., B.S., D.Sc., 1
Franklin, K. J., D.M. Valves in Veins: further observations, 67

Garde, Mary Lee, B.Sc. The Ovary of *Ornithorhynchus*, with special reference to Follicular Atresia, 422
Gates, R. Ruggles. Heredity in Man. Review, 541
von Gierke, Prof. Dr Med. E. Taschenbuch der Pathologischen Anatomie. 10th edition, 1929, vols. 1–2. Review, 104

Gilmour, J. Obstruction of the urethra by prostatic valves, 124
Gladstone, Reginald J., M.A., F.R.C.S. Axillary Mamma in a Man, 239
— Development of the Inferior Vena Cava in the light of recent research, with especial reference to certain abnormalities, and current descriptions of the Ascending Lumbar and Azygos Veins, 70, 111
Glands, Cutaneous, of Man. By H. H. Woollard, 415
Gorilla, Pterion of, note on a rare type of. By M. F. Ashley-Montagu, 247
Green, Prof. An abnormal cavum septum pellucidi, 128
Green, H. L. A description of the Egg Tooth of *Ornithorhynchus*, together with some notes on the development of the Palatine processes of the Premaxillae, 512
De Grzybowski, J. et R. Anthony. Le *neopallium* des équidés. Étude du développement de ses plissements, 147

Harris, H. A., D.Sc., M.B., B.S. Cystic Ovary in a Babe aged two months, 303
— The Diploic Veins as evidence of age, with especial reference to the skull attributed to Lord Darnley, 115
— The growth of the Long Bones in Foetal Life, as exemplified by a case of Foetal Syphilis, 1
— The Vascular supply of Bone, with special reference to the Epiphysial Cartilage, 3, 123
Heart, Bird's, conducting system of the. By Francis Davies, M.D. (Lond.), 129. Further studies, 319
— two-chambered. By Prof. William Wright, 120
Heiderich, Peter and Wetzel. Handbuch der Anatomie des Kindes. Zweiter Band, 2 Lieferung. Review, 536
Hermaphrodite Pig, Histology of the Gonads of. By Dr F. W. Brambell, 111
Hess, Alfred F. Rickets, including Osteomalacia and Tetany. Review, 539
Hewer, E. E. and G. M. Sandes. Introduction to the Study of the Nervous System. Review, 535
Hewitt, R. W. Anatomical Note. An abnormal left Bronchial Artery, 363
Hill, Prof. J. P., and Dr G. S. Sansom. Observations on the Structure and mode of Implantation of the Blastocyst of Cavia, 113
Hill, W. C. Osman, M.D., Ch.B. (Birm.). Observations on the growth of the Suprarenal Cortex, 479
Honan, Dr M. S. Some notes on the early Adrenals, 194
Horse. Le *neopallium* des équidés. Étude du développement de ses plissements. By R. Anthony et J. De Grzybowski, 147
Human Embryos, young, the formation of the connecting stalk and the extension of the Amniotic Cavity towards the tissue of the connecting stalk in young Human Embryos. By J. Florian, M.D., 454
Hydronephrosis, Aberrant accessory Ureter associated with. By Harold Edwards, M.S., F.R.C.S., 94

Ilium, Note on the architecture of. By Cecil Wakeley, 109
Insectivores, Thalamus in, anterior nuclei of. By Prof. Le Gros Clark, 125

Jones, Frederic Wood, F.R.S. Man's Place among the Mammals. Review, 531
Jutish Skulls, observations on. By Prof. Parsons, 120

Kappers, Ariëns. The brain of Fossil Animals—a review, 254
Keith, Sir Arthur. Comité International des recherches des parties molles (Parties non osseuses), 99
Kidney, fused pelvic, found in a Bantu Native of South Africa. Report on specimen. By L. R. Shore, M.A., M.B., M.R.C.P., D.P.H., 344
Kuntz, Albert, Ph.D., M.D. The Autonomic Nervous System. Review, 537

Llama, female, Notes on. By W. C. McIntosh, M.D., D.Sc., LL.D., F.R.S., 353
Lockhart, Robert D., Ch.M. Complete double Aortic Arch, 189
— Movements of the normal shoulder joint and of a case with Trapezius paralysis studied by radiogram and experiment in the living, 124, 288
Lung, Right, showing only one fissure. By Dr E. P. Stibbe, 127
Lymphatic plexuses, Method of demonstrating. By Prof. W. E. Le Gros Clark, 115

Macacus, Man and Orang, Anomalies of sixth Cervical Vertebra in. By A. J. E. Cave, M.B., 118
McIntosh, W. C., M.D., D.Sc., LL.D., F.R.S. Notes on a female Llama, 353
Mackay, John Yule, Obituary notice of. By D. Rutherford Dow, 529
Macula, cortical representation of. By G. Elliot Smith, F.R.S., 477
Mainland, Donald, M.B., Ch.B. (Edin.). The early development of the Ferret: the Pronuclei, 262
Mamma, Axillary, in a Man. By R. J. Gladstone, M.D., F.R.C.S., 239
Mammary Artery, Internal, Lateral thoracic branch of. By Dr E. P. Stibbe, 127
Man, Axillary Mamma in. By R. J. Gladstone, M.D., F.R.C.S., 239
— Cutaneous Glands of. By H. H. Woollard, 415
— Orang and *Macacus*, anomalies of sixth Cervical Vertebra in. By A. J. E. Cave, M.B., 118
Mandible, Human, at the 17 mm. C.R. Stage; model of the Left Half. By Prof. Fawcett, M.D., F.R.S., 369
Maxillary Sinuses, asymmetrical, Skull showing a cranio-pharyngeal canal and. By A. J. E. Cave, M.B., 126

Mesenteric Circulation, Observations on. By A. J. Cokkinis, M.B., B.S. (Lond.), F.R.C.S. (Eng.), 200
Mookerji, P. D., I.M.S., and Capt. B. S. Nat, M.B., Ch.B., F.R.C.S., I.M.S. Abnormal Duodenum, 250
Muscle, quadratus femoris, Complete absence of. By Dr E. P. Stibbe and Dr F. Davies, 119
Muscles, masticatory and hyoid, of larvae of *Xenopus Laevis*. By F. H. Edgeworth, M.D., 184
— palato-pharyngeus and superior constrictor, Arrangement of. By J. Whillie, 123

Nat, Capt. B. S., M.B., Ch.B., F.R.C.S., I.M.S., and P. D. Mookerji, I.M.S. Abnormal Duodenum, 250
Negus, V. E. Function of the Cartilages of Santorini, 111
Neopallium des équidés. Étude du développement de ses plissements. By R. Anthony et J. De Grzybowski, 147
Nerves. Communicating branches between the Cervical Sympathetic and the descendens cervicalis. By Alvaro Rodrigues, 308
— Motor, of the Eye, Sensory components of. By E. P. Stibbe, 112

Orang, Man and *Macacus*, Anomalies of sixth Cervical Vertebra in. By A. J. E. Cave, M.B., 118
Ornithorhynchus, Egg Tooth of, description of, together with some notes on the development of the Palatine processes of the Premaxillae. By H. L. Green, 512
— Ovary of, with special reference to Follicular Atresia. By Mary Lee Garde, B.Sc., 422
Ovary, Cystic, in a Babe aged two months. By H. A. Harris, D.Sc., M.B., B.S., 303
— of *Ornithorhynchus*, with special reference to Follicular Atresia. By Mary Lee Garde, B.Sc., 422

Palato-pharyngeus and superior constrictor muscles, Arrangement of. By J. Whillie, 123
Papez, James W. Comparative Neurology. Review, 540
Parkes, A. S. The Internal Secretions of the Ovary. Review, 538
Parkes, U. W. A. A Text-book on the Artistic Anatomy of the Human Form. Review, 535
Parsons, Prof. Some observations on Jutish Skulls, 120
Paterson, R. S., M.D., D.M.R.E. A Radiological investigation of the Epiphyses of the Long Bones, 28
Patten, C. J. Technique of Bird utterances, 108
Penis, double, below an ectopia vesicae. Case of. By Ralph Thompson, 121
Peter, Wetzel and Heiderich. Handbuch der Anatomie des Kindes. Zweiter Band, 2. Lieferung. Review, 536
Pig, Hermaphrodite, Histology of the Gonads of. By Dr F. W. Brambell, 111
Premaxillae, Palatine processes of. Description of the Egg Tooth of *Ornithorhynchus*, together with some notes on the development of. By H. L. Green, 512
Pterion in the Gorilla, Note on a rare type of. By M. F. Ashley-Montagu, 247

Quadratus Femoris, Complete absence of. Anatomical Notes by E. P. Stibbe, 97
Quadratus femoris muscle, Complete absence of. By Dr E. P. Stibbe and Dr F. Davies, 119

Reviews. A Text-book of Artistic Anatomy of the Human Form. By U. W. A. Parkes, 535
— Anatomy and the problem of Behaviour. Lectures delivered at University College, London. By G. E. Coghill, 1929, 104
— Ballière's Synthetic Anatomy. Part v, The Leg. Part vi, The Foot. By J. E. Cheesman, 537
— Comparative Neurology. By James W. Papez, 540
— Handbuch der Anatomie des Kindes. Zweiter Band, 2. Lieferung. By Peter, Wetzel and Heiderich, 536
— Heredity in Man. By R. Ruggles Gates, 541
— Introduction to the Study of the Nervous System. By E. E. Hewer and G. M. Sandes, 535
— Man's Place among the Mammals. By Frederic Wood Jones, F.R.S., 531
— Rickets, including Osteomalacia and Tetany. By Alfred F. Hess, 539
— Taschenbuch der Pathologischen Anatomie. By Prof. Dr Med. E. von Gierke. 10th edition, 1929, vols. 1–2, 104
— The Autonomic Nervous System. By Albert Kuntz, Ph.D., M.D., 537
— The Internal Secretions of the Ovary. By A. S. Parkes, 538
— Vertebrate Zoology. An Introduction to the Comparative Anatomy, Embryology and Evolution of Chordate Animals. By G. R. de Beer, with an Introduction by Julian S. Huxley, 534
Rodrigues, Alvaro. Communicating branches between the Cervical Sympathetic and the descendens cervicalis, 308
Rogers, Lambert, M.Sc., F.R.C.S., F.A.C.S. The Thyroid Arteries considered in relation to their surgical importance, 50
Rutherford, R. Case of undescended testicle associated with Uterus and Fallopian tube, 121

Sacro-iliac Synostosis, developmental, specimen of. By L. R. Shore, M.A., M.B., M.R.C.P., D.P.H., 503
Sandes, G. M. and E. E. Hewer. Introduction to the Study of the Nervous System. Review, 535
Sansom, Dr G. S., and Prof. J. P. Hill. Observations on the structure and mode of Implantation of the Blastocyst of Cavia, 113
Santorini, Cartilages of, function. By V. E. Negus, 111

Shore, L. R., M.A., M.B., M.R.C.P., D.P.H. Abnormalities of the Vertebral Column in a series of skeletons of Bantu Natives of South Africa, 206
— A Report on a specimen of fused pelvic kidney found in a Bantu Native of South Africa, 344
— A specimen of developmental Sacro-iliac Synostosis, 503
Shoulder joint, abnormal. By Prof. Thomas Walmsley, 120
— Normal, movements of, and of a case with Trapezius paralysis studied by radiogram and experiment in the living. By R. D. Lockhart, Ch.M., 124, 288
Skeletons of Bantu Natives of South Africa, Abnormalities of the Vertebral Column in. By L. R. Shore, M.A., M.B., M.R.C.P., D.P.H., 206
Skull showing cranio-pharyngeal canal and asymmetrical maxillary sinuses. By A. J. E. Cave, M.B., 126
Skulls, Jutish, Observations on. By Prof. Parsons, 120
Smith, G. Elliot, F.R.S. The cortical representation of the Macula, 477
— Obituary notice. Sir George Dancer Thane. *Portrait*, 364
South Africa, Bantu Native of. Report on a specimen of fused pelvic kidney found in. By L. R. Shore, M.A., M.B., M.R.C.P., D.P.H., 344
— Bantu Natives, abnormalities of the Vertebral Column in a series of skeletons of. By L. R. Shore, M.A., M.B., M.R.C.P., D.P.H., 206
Stibbe, Dr E. P. Anatomical Notes. A Bursal Sac in the substance of the Subscapularis, 98
— — Complete absence of the Quadratus Femoris, 97
— Lateral thoracic branch of the Internal Mammary Artery, 127
— Right Lung showing only one fissure, 127
— Sensory components of the Motor Nerves of the Eye, 112
— True congenital diverticulum of the Trachea in a subject showing also right Aortic Arch, 62
— and Dr F. Davies. Complete absence of the quadratus femoris muscle, 119
— — Bursal Cyst in subscapularis (?), 119
Stopford, John S. B., F.R.S. The functional significance of the arrangement of the Cerebral and Cerebellar Veins, 257
Submaxillary Gland. The presence of deep Submaxillary Lymph Glands in the substance of the Submaxillary Salivary Gland. By Prof. D. M. Blair, 111
Subscapularis (?), Bursal Cyst in. By Dr E. P. Stibbe and Dr F. Davies, 119
— Bursal Sac in the substance of. Anatomical Notes. By E. P. Stibbe, 98
Suprarenal Cortex, Observations on the growth of. By W. C. Osman Hill, M.D., Ch.B. (Birm.), 479
Synostosis, Sacro-iliac, developmental, specimen of. By L. R. Shore, M.A., M.B., M.R.C.P., D.P.H., 503
Syphilis, Foetal. The growth of the Long Bones in Foetal Life, as exemplified by a case of Foetal Syphilis. By H. A. Harris, M.B., B.S., D.Sc., 1

Tarsius, Thalamus of. By W. E Le Gros Clark, 371
Testicle, undescended, associated with Uterus and Fallopian tube. By R. Rutherford, 121
Testis, retained, Histology of, in the human subject at different ages, and its comparison with the Scrotal Testis. By Eugenia R. A. Cooper, M.D., M.Sc., 5
Thalamus in Insectivores, anterior nuclei of. By Prof. Le Gros Clark, 125
— of *Tarsius*. By W. E. Le Gros Clark, 371
Thane, Sir George Dancer. Obituary notice. By G. Elliot Smith, 364
Thompson, Ralph. Case of double penis below an ectopia vesicae, 121
Thyroid Arteries considered in relation to their surgical importance. By Lambert Rogers, M.Sc., F.R.C.S., F.A.C.S., 50
Trapezius, paralysis of. Movements of the normal shoulder joint and of a case with trapezius paralysis studied by radiogram and experiment in the living. By R. D. Lockhart, Ch.M., 124, 288

Urachus, anatomy, histology and development of. By R. Campbell Begg, M.C., M.A., M.Sc., M.D., Ch.B., F.R.C.S. (Edin.), M.R.C.S. (Eng.), L.R.C.P. (Lond.), F.A.C.S., F.C.S.A., 170
Ureter, Aberrant Accessory, associated with Hydronephrosis. By Harold Edwards, M.S., F.R.C.S., 94
Urethra, Obstruction of, by prostatic valves. By J. Gilmour, 124
Uterus and Fallopian tube, Case of undescended testicle associated with. By R. Rutherford, 121

Valves in Veins: Further observations. By K. J. Franklin, D.M., 67
Veins, Cerebral and Cerebellar, functional significance of the arrangement of. By John S. B. Stopford, F.R.S., 257
— Lumbar and Azygos, Development of the Inferior Vena Cava in the light of recent research, with especial reference to certain abnormalities, and current descriptions of the Ascending Lumbar and Azygos Veins. By Reginald J. Gladstone, M.D., F.R.C.S., 70, 111
— Valves in: further observations. By K. J. Franklin, D.M., 67
Vena Cava, Inferior, Development of, in the light of recent research, with especial reference to certain abnormalities, and current descriptions of the Ascending Lumbar and Azygos Veins. By Reginald J. Gladstone, M.D., F.R.C.S., 70, 111
Vertebra, sixth Cervical, anomalies in Man, Orang and *Macacus*. By A. J. E. Cave, M.B., 118

Vertebrae, Atlas and Axis, fusion of. By A. J. E. Cave, M.B., 337
— Cervical, fusion of third and fourth. By A. J. E. Cave, M.B., 118
Vertebral column, Abnormalities of, in a series of skeletons of Bantu Natives of South Africa. By L. R. Shore, M.A., M.B., M.R.C.P., D.P.H., 206

Wakeley, Cecil P. G., F.R.C.S. (Eng.), F.R.S. (Edin.). Congenital Atresia of the Duodenum, 527
— Note on the architecture of the Ilium, 109
Walmsley, Prof. Thomas, M.D. An abnormal shoulder joint, 120
— A diverticulum of the Appendix, 47
West, Prof. C. M. Two unusual abnormalities of the flexor pollicis longus, 126
Wetzel, Peter and Heiderich. Handbuch der Anatomie des Kindes. Zweiter Band, 2. Lieferung. Review, 536
Whillie, J. Arrangement of the fibres of the palato-pharyngeus and superior constrictor muscles, 123
Woollard, H. H. The Cutaneous Glands of Man, 415
Wright, Prof. William. Two-chambered heart, 120

Xenopus Laevis, Masticatory and hyoid muscles of larvae of. By F. H. Edgeworth, M.D., 184

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Volume XX. No. 2

CONTENTS

Kennedy, Walter P., and K. N. Flint. Studies on the Arneth Count. XIV. The Count in Surgical Tuberculosis in the High Alps.—Crew, F. A. E., and L. Mirskaia. The Lactation Interval in the Mouse.—Masters, A. H. Description of a Self-recording Water Manometer.—Simpson, Ethel D., and W. H. Finney. The Effect of Acids and their Salts on Heat Contraction of Rat Tendon.—Elvidge, A. R. Non-specific Changes in the Opsonic Power of Rabbit Serum produced physically through the Intravascular Injection of Foreign Particles in Suspension.—Danzer, M. Studies on the Arneth Count. XV. The Effect of Tissue Injury.—Macwilliam, J. A. The Action of the Vagus Nerve on the Mammalian Heart.—Climenko, D. R. Studies on the Arneth Count. XVI. The Deflection of the Count by Irradiated Ergosterol.

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CONTENTS

VOLUME XLIV

PAGE

PROFESSOR FAWCETT, M.D., F.R.S. A Study of the Left Half of the Human Mandible and its Variations, Compared with Those of Some Allied Species (with 2 Text-figures) 369

W. E. LE GROS CLARK. The Thalamus of Tupaia (with 23 Text-figures and Plates I and II) 371

H. H. WOOLLARD. The Cutaneous Glands of Man 415

MARY LEE GARDE, B.Sc. The Ovary of *Ornithorhynchus*, with special reference to Follicular Atresia (with Plates [illegible]) 422

J. FLORIAN, M.D. The Formation of the Connecting Stalk and the Extension of the Amniotic Cavity towards the Base of the Connecting Stalk in Young Human Embryos (with 15 Text-figures and Plates I–III) 456

G. ELLIOT SMITH, F.R.S. The Cortical Representation of the Macula (with 2 Text-figures) 477

W. C. OSMAN HILL, M.D., Ch.B. (Brux.). Observations on the Growth of the Suprarenal Cortex (with 3 Text-figures) 479

L. R. SHORE, M.A., M.B., M.R.C.P., D.P.H. An Account of Developmental Sacro-Iliac Synostosis (with 3 Text-figures) 503

H. L. GREEN. A Description of the Egg Tooth of *Ornithorhynchus*, together with some Notes on the Development of the Palatine Processes of the Premaxillae (with 2 Text-figures and Plate I) 512

CHARLES DONALD, F.R.C.S. A Case of Human Diphallus (with 4 Text-figures) 523

CECIL P. G. WAKELEY, F.R.C.S. (Eng.), F.R.S. (Hon.). Congenital Atresia of the Duodenum (with 1 Text-figure) 527

OBITUARY NOTICE (with Photograph): The Late Principal John Yule Mackay 529

REVIEWS: *Man's Place among the Mammalia*. By [illegible] Wood Jones, F.R.S. *Vertebrate Zoology*. By G. R. de Beer. *Evolution*. By Julian S. Huxley 531

A Text-Book on the Artistic Anatomy of the Human Form. By U. W. A. Parkes 534

Introduction to the Study of the Nervous System. By E. B. Fawcett and G. M. Sanders 535

Handbuch der Anatomie des Kindes. By Peiper, Wetzel and Heinerich 535

Ballière's Synthetic Anatomy. By J. E. Cleminson 536

The Autonomic Nervous System. By Albert Kuntz, Ph.D., M.D. 537

The Internal Secretions of the Ovary. By A. S. Parkes 537

Rickets, including Osteomalacia and Tetany. By Alfred F. Hess 538

Comparative Neurology. By James W. Papez 539

Heredity in Man. By R. Ruggles Gates 540

INDEX 541

543

INSTRUCTIONS TO CONTRIBUTORS

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5. A contribution should terminate with a brief summary of the chief descriptions or observations and any conclusions drawn therefrom.

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